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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 21

June 5, 1992



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This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.

NOTICES

THE NATIONAL CELL CULTURE CENTER

NIH GUIDE, Vol, 21, No. 21, June 5, 1992

P.T. 34; K.W. 0780005, 0780015

National Center for Research Resources

The National Cell Culture Center is a resource facility that provides large-scale mammalian cell culture services. The Center, available to researchers throughout the United States, has been established to alleviate the current shortage of facilities and expertise required to meet the cell culture needs of the biomedical research community.

Specifically, the Cell Culture Center supports basic research by providing investigators with the following customized services:

- o Large quantity production of mammalian cells in suspension or monolayer cultures. Quantities range from 10 to 150 liters.



o Large quantity production of monoclonal antibodies. Quantities range from 0.5 to 100 grams.

o Large quantity production of non-hybridoma cell secreted proteins. Quantities vary depending on individual cell lines.

An application form, obtained from the Cell Culture Center, must contain a description of the relevant research project. Following approval of the application by the Cell Culture Center's Scientific Advisory Board, the applicant's cell line is sent to the Center, and grown to the requested amount. Researchers are charged only for the consumable materials and a portion of the labor costs required for each project.

The Cell Culture Center is supported by a cooperative agreement award from the National Center for Research Resources, NIH.

#### INQUIRIES

Programmatic inquiries regarding this research resource are encouraged and are to be directed to:

Biological Models and Materials Research Program  
National Center for Research Resources  
Westwood Building Room 8A07  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-9840

Application forms may be requested from:

Director, National Cell Culture Center  
8500 Evergreen Boulevard  
Minneapolis, MN 55433  
Telephone: 1-800-325-1112

#### REMINDER AND REVISION OF RECEIPT DATES

NIH GUIDE, Vol. 21, No. 21, June 5, 1992

P.T. 34; K.W. 1002002, 070000

National Center for Research Resources

The Notice, "Reminder of Receipt Dates" that recently appeared in the NIH Guide for Grants and Contracts (Vol. 21, No. 17, May 8, 1992) incorrectly identified the title of the program for which applications were to be received by June 1. The correct title is "Animal Facility Improvement for Small Research Programs." Because of the confusion resulting from the May 8 Notice, the receipt date for these applications has been changed from June 1 until August 1, 1992, on a one-time basis. The single deadline of October 1 for applications for "Developing and Improving Institutional Animal Resources" remains unchanged.

Copies of the announcement and updated application guidelines, which reflect special instructions to accompany the form PHS 398 (rev. 9/91), may be obtained by sending two self-addressed mailing labels to:

Comparative Medicine Program  
National Center for Research Resources  
Westwood Building, Room 857  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-5175

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### ESTABLISHMENT OF A DNA BANK

NIH GUIDE, Volume 21, Number 21, June 5, 1992

RFP AVAILABLE: NIH-ES-92-28

P.T. 34; K.W. 0780030, 0760053

National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences, National Institutes of Health, is soliciting proposals from offerors having the capability to operate a DNA Bank. This requirement is divided into two parts: (1) DNA Extraction and (2) Specimen Storage and Inventory. The Government estimates the project will last approximately 24 months and will require approximately 416 senior professional person-hours, 8,300 professional person-hours and 1040 technical person-hours. The Request for Proposals (RFP) will be released on or about May 27, 1992, and proposals are due to be received by July 15, 1992. All responsible sources may submit a proposal that shall be considered by the Agency.



Requests must reference RFP NIH-ES-92-28 and are to be forwarded to:

National Institute of Environmental Health Sciences  
Contracts and Procurement Management Branch  
ATTN: Mr. James Doyle, Contract Specialist  
79 T.W. Alexander Drive, 4401 Research Commons Building  
P.O. Box 12874  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7893

HORMONAL REGULATION OF BONE IN HEALTH AND DISEASE

NIH GUIDE, Volume 21, Number 21, June 5, 1992

RFA AVAILABLE: DK-92-20

P.T. 34; K.W. 0705050, 0760025, 0775000

National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: July 10, 1992  
Application Receipt Date: August 25, 1992

NOTE: THE FULL TEXT OF THE REQUEST FOR APPLICATIONS (RFA) SHOULD BE REQUESTED - SEE INQUIRIES SECTION.

PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the NIAMS invite investigator-initiated research grant applications to elucidate the role(s) of systemic and local hormones, growth factors, and cytokines on bone in health and disease.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and nonprofit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Minority individuals and women are encouraged to submit as Principal Investigators.

MECHANISM OF SUPPORT

Support of this program will be through the NIH research project (R01) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this announcement, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and reviewed according to the customary peer review procedures. The total project period for applications submitted in response to the present RFA may not exceed five years. A maximum of three years may be requested for foreign awards. The earliest possible award date will be April 1, 1993.

FUNDS AVAILABLE

For FY 93, the NIDDK intends to commit \$2,000,000 to fund applications submitted in response to this RFA and the NIAMS intends to commit a further \$2,000,000 to this RFA. However, this funding level is dependent upon the receipt of a sufficient number of applications of high scientific merit. In order to help meet NIH goals for managing the costs of biomedical research, applicants must limit requests to not more than \$160,000 direct costs for the initial budget period. Although this program is provided for in the financial plans of the NIDDK and the NIAMS, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

RESEARCH OBJECTIVES

This initiative is intended to foster research on the molecular mechanisms of action of hormones and related factors on a major endocrine target organ: bone. This research will advance the understanding of the molecular mechanisms by which hormones regulate normal growth and homeostasis of bone and how alterations in hormonal status cause disease. Ultimately, such research may lead to design of hormone analogs with specific desirable properties for therapy of bone disorders based on new understandings of molecular endocrinology.



## SPECIAL REQUIREMENTS

Interdisciplinary approaches may be needed for these studies with expertise required in one or more of the following areas: molecular and cellular biology, endocrinology, physiology, pathology, and pharmacology.

## STUDY POPULATIONS

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them, and the study design must seek to identify any pertinent gender or minority population differences.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by July 10, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDDK staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

A letter of intent is to be sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083

## APPLICATION PROCEDURES

Applications are to be submitted using form PHS 398 (rev. 9/91) available in the business or grants offices of most academic or research institutions and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496- 7441.

## REVIEW CONSIDERATIONS

Applications that are complete and responsive to the RFA will be evaluated by an appropriate peer review group convened by the NIDDK in accordance with the usual NIH peer review procedures. Following review, the applications will be given a secondary review by the NIDDK and NIAMS Advisory Councils unless not recommended for further consideration by the initial review group. Applications that are incomplete or unresponsive to the RFA will be returned to the applicant or held until the next receipt date, if requested by the applicant, and reviewed by the Division of Research Grants.

The National Institute on Aging (NIA), and the National Institute of Dental Research (NIDR) also have an interest in supporting areas of research covered by this RFA. The PHS Referral Guidelines will prevail in the institute assignment of applications.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. Direct inquiries regarding programmatic issues and requests for copies of the RFA should be directed to:

Ronald N. Margolis, Ph.D.  
Endocrinology Research Program  
Division of Diabetes, Endocrinology and Metabolic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 621  
Bethesda, MD 20892  
Telephone: (301) 496-7504

Joan A. McGowan, Ph.D.  
Chief, Bone Biology and Bone Diseases Branch  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 480-7881



Direct inquiries regarding fiscal matters to:

Sharon Tempchin  
Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
5333 Westbard Avenue, Room 649D  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.847 and 93.846. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### CONTEMPORARY APPROACHES TO OVARIAN CANCER BIOLOGY RESEARCH

NIH GUIDE, Volume 21, Number 21, June 5, 1992

RFA AVAILABLE: CA-92-18

P.T. 34; K.W. 0715035, 0755030, 1002004, 1002008

National Cancer Institute

Letter of Intent Receipt Date: July 17, 1992

Application Receipt Date: October 9, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Cancer Biology Branch of the Division of Cancer Biology, Diagnosis, and Centers (DCBDC) of the National Cancer Institute (NCI) invites applications for grants to study the basic tumor biology of ovarian cancer of epithelial and non-epithelial origin. Although interest in research on these malignancies has increased somewhat in the past several years, there remains a significant lack of understanding about the underlying factors, both intrinsic (genetic and cellular) and extrinsic (epigenetic), that contribute to the development of ovarian cancer. This initiative is designed to foster the application of recent advances in molecular and cellular biology, particularly those that use cells derived from samples of normal and malignant human tissues or that aid in the development and use of animal models, to study the generation and spread of ovarian malignancies.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), Contemporary Approaches to Ovarian Cancer Biology Research, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone (202) 783-3238.

#### ELIGIBILITY REQUIREMENTS

Research grant applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

Support of this RFA will be by National Institutes of Health (NIH) individual research grants (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed four years. The anticipated award date will be August 1, 1993.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary NIH peer review procedures.

#### FUNDS AVAILABLE

Approximately \$1,500,000 in total costs per year for four years will be committed to fund applications submitted in response to this RFA. It is anticipated that eight to ten awards will be made. This level of support is dependent on the receipt

of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

Ovarian cancer is the fourth leading cause of cancer deaths in women. If detected at an early stage, these malignancies respond well to therapy. However, because early detection is difficult, the malignancies are frequently at an advanced stage when discovered; consequently, many affected women succumb to the disease.

The Cancer Biology Branch supports a spectrum of basic research on how cancer cells differ from the normal counterparts, and progression from early neoplastic changes to greater degrees of malignancy. These studies range from investigation of the molecular biology of human and animal tumor cell behavior to analysis of cells in the context of the tissue of origin or the tissue in an animal model. This research may ultimately help to pinpoint steps in the malignant process at which therapeutic intervention is possible and to identify markers for detection, diagnosis, and prognosis.

The base of information about the biology of ovarian cancer is limited, and few facts about its development, particularly at the early stages, are known. However, the preliminary observations about ovarian cancer suggest many intriguing features that are unique to these malignancies. Information is needed about the intrinsic and extrinsic factors that contribute to the development of ovarian malignancies. The potential now exists to apply the techniques used for the study of other solid tumors to ovarian cancer to begin to establish a foundation of basic knowledge about this disease. This RFA is intended to encourage a variety of investigator-initiated research projects. It may include collaborations among basic and clinical scientists, and it likely will embrace an array of molecular and cellular approaches. Evidence of the establishment of reliable cellular systems or relevant models should be included in the applications.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

The following is a statement of NIH and ADAMHA policy regarding the inclusion of women and minorities in study populations. Applications that are responsive to this RFA will, by definition, meet the requirement for inclusion of women. The inclusion of minorities must be addressed in applications submitted responding to this RFA.

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by July 17, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Cheryl L. Marks  
Program Director for Molecular Biology  
Tumor Biology Program  
Division of Cancer Biology, Diagnosis, and Centers  
National Cancer Institute  
Executive Plaza South, Room 630  
Bethesda, MD 20892-9904\*  
Telephone: (301) 496-7028  
FAX: (301) 402-1037

\*Applicants who use express mail or a courier service are advised to use the following street address:

Executive Plaza South, Room 630  
6120 Executive Blvd.  
Rockville, MD 20852

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892-9912, telephone (301) 496-7441.

Applications must be received by October 9, 1992. If an application is received after that date, it will be returned to the applicant without review.



#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants for completeness. Incomplete applications will be returned to the applicant without further consideration. Complete applications will be evaluated by NCI program staff to determine responsiveness to the program requirements and criteria stated in this RFA. If the application is not responsive to the RFA, NCI staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

If the number of applications is large compared to the number of awards to be made, NCI may conduct a preliminary scientific peer review to eliminate those that are clearly not competitive. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board considers the special needs of the Institute and the priorities of the National Cancer Program.

#### AWARD CRITERIA

The anticipated date of award is August 1, 1993. In addition to the technical merit of the application, NCI will consider how well the proposed research meets the goals and objectives of the program as described in the RFA.

#### INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA and inquiries about whether or not specific proposed research would be responsive are strongly encouraged and should be directed to the program director listed below. NCI program staff welcome the opportunity to clarify any issues or questions from potential applicants.

Direct inquiries regarding program issues to:

Dr. Cheryl L. Marks  
Program Director for Molecular Biology  
Tumor Biology Program  
Division of Cancer Biology, Diagnosis, and Centers  
National Cancer Institute  
Executive Plaza South, Room 630  
Bethesda, MD 20892  
Telephone: (301) 496-7028  
FAX: (301) 402-1037

Direct inquiries regarding fiscal and administrative matters to:

Mr. Robert Hawkins  
Grants Management Branch  
National Cancer Institute  
Executive Plaza South, Room 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800, ext. 13

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.396, Cancer Biology. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### BOWEL AND BLADDER MANAGEMENT

NIH GUIDE, Volume 21, Number 21, June 5, 1992

RFA AVAILABLE: HD/NR-93-05

P.T. 34; K.W. 0705025, 0705075, 0765035

National Institute of Child Health and Human Development  
National Center for Nursing Research

Application Receipt Date: August 7, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The National Center for Medical Rehabilitation Research, the National Institute of Child Health and Human Development (NICHD), and the National Center for Nursing Research (NCNR) invite research grant applications to develop new knowledge in the area of management of bowel and bladder functioning following disease, injury, and congenital conditions that alter normal function. The goal of this RFA is to encourage research that may lead to enhanced functioning of bowel and bladder and to improved management techniques for the treatment and care of the dysfunctional bowel and bladder. Interdisciplinary, collaborative projects that focus on bowel or bladder function are encouraged.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention goals of "Healthy People 2000," a PHS-led national activity for setting priorities. This RFA, Bowel and Bladder Management, is related to the priority areas of nutrition, physical activity and fitness, heart disease and stroke, cancer, diabetes, and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-474-0), or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone (202) 783-3238.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, public and private nonprofit and for-profit organizations such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply.

## MECHANISM OF SUPPORT

The support mechanism for this RFA is the individual research grant (R01). Policies that govern are those of the grant-in-aid award programs covered by the PHS.

Project support may be requested for between one and five years and may be renewed according to the conventional procedures that pertain to PHS grants-in-aid.

## FUNDS AVAILABLE

Applications submitted in response to this announcement will compete for approximately \$1,000,000 in grant money that has been made available for this purpose in Fiscal Year 1993. It is expected that four to six awards will be made. The number of awards depends upon the overall scientific merit of the applications, the relevance to the stated goal of the announcement, and the availability of funds.

## RESEARCH OBJECTIVES

This RFA invites scientists to submit grant applications for research that will lead to better understandings of the normal and dysfunctional bladder and bowel, restitution of function, and improvement in current management techniques. Development of new management strategies should consider such factors of the individual as work environment, recreational life, travel, geographic location, and access to medical assistance. The list of research areas cited below is representative, not exhaustive, of the topics solicited by this announcement and shall serve as a guide for applicants submitting a response to this RFA.

- o improved test parameters and classification schema for neurogenic bowel and bladder
- o bowel and bladder self-care techniques for populations with other impairment (cognitive limitation or mobility impairment), such as those with spina bifida, hydrocephalus, or quadriplegia
- o development of outcome measures of the effectiveness of management programs
- o assessment of management procedures for children and elderly adults with disabilities including adherence to management techniques and impact on social integration
- o new design of urine collection devices for females with disabilities and assessment of optimal bladder management in females
- o identification and resolution of management problems in females with disabilities during pregnancy, childbirth, and postpartum
- o physiological changes associated with aging with a disability or with the duration of impairment and the effect on bowel and bladder management
- o improved techniques for treatment of detrusor-sphincter dyssynergia; assessment of long-term morbidity following sphincterectomy
- o assessment of the use of tests for pyuria in identifying bacteriuric individuals who require treatment for urinary tract infection
- o mechanisms of bacterial adherence to catheter and bladder; development of interventions



o improved methods for localizing site of urinary tract infection in paralyzed individuals; especially for those with sepsis or kidney involvement

o assessment of use of cranberry juice, ascorbic acid, or distilled water to prevent urinary tract infection in spinal cord injured people

o criteria for failed conservative management and long-term assessment of bowel or bladder diversion procedures

o long-term evaluation of treatments for gastroenteritis and lower bowel dysfunctions, including assessment of levels of function, impairment, and disability

o assessment of physiologic effectiveness, and the impact on lifestyle, of the use of pharmacologic treatments for bowel and bladder care

o control and management of autonomic dysreflexia through bowel and bladder management

o neurologic mechanisms of control of bowel or bladder function in the impaired state as related to a rehabilitation treatment approach

o evaluation of neuromuscular prosthetics or orthotics for management of bladder or bowel and testing of physiologic effectiveness and acceptance by user for activities of daily living

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a special justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91). This application form is available in the business or grants and contracts office at most academic and research institutions and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The receipt deadline for applications prepared in response to this RFA is August 7, 1992. Late applications will be returned to the applicant without review.

#### REVIEW CONSIDERATIONS

Applications will be reviewed by staff of the NICHD staff for responsiveness to the RFA. Applications deemed non-responsive will be returned to the applicant. In the event that an application is returned, the applicant has the option to resubmit the application to the Division of Research Grants as an unsolicited application during one of the three yearly review cycles (February 1, June 1, and October 1).

Responsive applications may be evaluated for a preliminary triage by a peer review group to determine scientific merit relative to other applications received in connection with this RFA. NICHD officials will withdraw from competition those applications judged to be non-competitive. The Principal Investigator and his/her institutional business official will be notified in such instances. Those applications judged to be competitive will be further evaluated for technical and scientific merit by a peer review panel convened for this purpose by the Division of Scientific Review, NICHD.

Review criteria will be those customarily used by NIH to evaluate investigator-initiated R01 applications.

Following evaluation by the initial review group, all applications will be reviewed by the National Advisory Child Health and Human Development Council or the National Advisory Council for Nursing Research.

#### INQUIRIES

Requests for additional information and descriptions of proposed research projects may be addressed to:

Cheryl M. Chanaud, Ph.D.  
Applied Rehabilitation Medicine Research Branch  
National Center for Medical Rehabilitation Research  
National Institute of Child Health and Human Development  
Executive Plaza South, Room 450W  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-2242

or

Laura A. James, Ph.D., R.N.  
Nurse Scientist Administrator  
Acute and Chronic Illness Branch  
National Center for Nursing Research  
Building 31, Room 5B03  
Bethesda, MD 20892  
Telephone: (301) 496-0523

For fiscal and administrative inquiries regarding this announcement, potential applicants may write or call:

E. Douglas Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 501  
6130 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 496-1303

or

Sally Nichols  
Grants Management Officer  
National Center for Nursing Research  
Building 32, Room 5B06  
Bethesda, MD 20892  
Telephone: (301) 496-0237

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.929, Medical Rehabilitation Research, and No. 93.335, Nursing Research. Awards are under made authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

#### RESEARCH AND DEMONSTRATION GRANTS RELATING TO OCCUPATIONAL SAFETY AND HEALTH

NIH GUIDE, Volume 21, Number 21, June 5, 1992

PA AVAILABLE: PA-92-83 (OH-92-923 (92-78))

P.T. 34; K.W. 0725020, 0403004

Centers for Disease Control  
National Institute for Occupational Safety and Health

MORE DETAILED INFORMATION IS PROVIDED IN THE COMPLETE PROGRAM ANNOUNCEMENT THAT MAY BE OBTAINED FROM THE CONTACTS NAMED IN "INQUIRIES."

#### PURPOSE

The National Institute for Occupational Safety and Health (NIOSH) is soliciting grant applications for research and demonstration projects relating to occupational safety and health.

The purposes of this grant program are to increase knowledge about the underlying characteristics of occupational safety and health problems in industry and on effective solutions in dealing with them; to eliminate or control factors in the work environment that are harmful to the health and/or safety of workers; and to demonstrate technical feasibility or application of a new or improved occupational safety and health procedure, method, technique, or system.

In 1983, the NIOSH published a suggested list of 10 leading work-related diseases and injuries as part of a national goal to improve the health of the American people through prevention activities. To provide guidance on priorities for action, the NIOSH sponsored the development of "Proposed National Strategies for the Prevention of Leading Work-Related Diseases and Injuries." Implementation of the Prevention Strategies requires commitment from a broad array of organizations and scientific and professional disciplines. The extramural research program is an important means of facilitating progress in these preventive efforts.

Additional guidance is found in the document, "Healthy People 2000: National Health Promotion and Disease Prevention Objectives." The document contains measurable objectives and strategies for creating a healthier society over the next decade. The objectives and strategies are organized broadly into three major categories: Health Promotion, Health Protection, and Preventive Services. There are a total of 22 priority areas. The tenth priority area, "Occupational Safety



and Health," is applicable to this program announcement. Overall objectives in this priority area are to reduce work-related deaths, injuries, and illnesses. Research is needed on the following: identification of new stressors affecting workers, new measurement tools for assessing worker exposures, biomarkers of workers' exposure and response, identification of populations and individuals at special risk of work-related disease and injury, mechanisms of insult and intoxication, hazard surveillance, disease and injury identification and surveillance, development of control approaches, and effective use of controls. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-0473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone (202) 783-3238.

#### ELIGIBILITY REQUIREMENTS

Eligible applicants include non-profit and for-profit organizations such as universities, colleges, research institutions, and other public and private organizations, including State and local governments. Small, minority and/or woman-owned businesses are eligible for these research and demonstration grants.

#### FUNDS AVAILABLE

The NIOSH anticipates that approximately \$6,747,847 is available for FY 1992 to fund these grants: \$4,078,575 for non-competing continuation awards and \$2,669,272 for new and competing renewal awards. The estimated distribution of funds for the new and competing renewal awards is as follows: R01 and R18 grants - 13 awards for \$2,160,772 (total costs of these awards range from \$50,000 to \$250,000 with the average award being about \$130,000); K01 grants - 4 awards for \$216,000; and R03 grants - 13 awards for \$292,500.

Grants are usually funded for 12-month budget periods in project periods up to 5 years for research project grants and demonstration project grants; 3 years for SERCA grants; and up to 2 years for small grants. Continuation awards within the project period are made on the basis of satisfactory progress and the availability of funds.

#### MECHANISM OF SUPPORT

The support mechanisms for this program are the individual research project grants (R01); demonstration project grants (R18); special emphasis research career award (SERCA) grants (K01); and small grants (R03).

**Individual Research Project Grant (R01):** These grants are designed to establish, discover, develop, elucidate, or confirm information relating to occupational safety and health, including innovative methods, techniques, and approaches for dealing with occupational safety and health problems. These studies may generate information that is readily available to solve problems or contribute to a better understanding of underlying causes and mechanisms.

**Demonstration Grant (R18):** These grants address, either on a pilot or full-scale basis, the technical or economic feasibility or application of: (a) a new or improved procedure, method, technique, or system; or (b) an innovative method, technique, or approach for preventing occupational safety or health problems.

**Special Emphasis Research Career Grant (SERCA) (K01):** These grants are intended to provide opportunities for individuals to acquire experience and skills essential to the study of work-related hazards, and in so doing, create a pool of highly qualified investigators who can make future contributions to research in the area of occupational safety and health. SERCA grants are not intended either for individuals without research experience or for productive, independent investigators with a significant number of publications and senior academic rank. Moreover, the award is not intended to substitute one source of salary support for another for an individual who is already conducting full-time research; nor is it intended to be a mechanism for providing institutional support.

Candidates must: (1) hold a doctoral degree; (2) have research experience at or above the doctoral level; (3) not be above the rank of associate professor; (4) be employed at a domestic institution; and (5) be a citizen or non-citizen national of the U.S. or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application.

This non-renewable award provides support for a three-year period for individuals engaged in full-time research and related activities. Awards will not exceed \$50,000 per year in direct costs for salary support (plus fringe benefits), technical assistance, equipment, supplies, consultant costs, domestic travel, publications, and other costs. The indirect cost rate applied is limited to eight percent of the direct costs, excluding tuition and related fees and equipment expenses, or to the actual indirect cost rate, whichever results in the lesser amount.

A minimum of 60 percent time must be committed to the proposed research project, although full-time is desirable. Other work in the area of occupational safety and health will enhance the candidate's qualifications but is not a substitute for this requirement. Related activities may include research career development activities and involvement in patient care to the extent that it will strengthen research skills. Fundamental/basic research will not be supported unless the project will make an original contribution for applied technical knowledge in the identification, evaluation, and/or control of occupational safety and health hazards (e.g., development of a diagnostic technique for early detection of an occupational disease). Research projects must be of the applicant's own design and of such scope that independent investigative capability will be evident within three years. At the completion of this three-year award, it is intended that awardees should be better able to compete for individual research project grants.

SERCA grant applications must be identified as such on the application form. Section 2 of the application (the Research Plan) must include a statement regarding the applicant's career plans and how the proposed research will contribute to a career in occupational safety and health research. This section must also include a letter of recommendation from the proposed

advisor(s) and a letter from the supporting institution agreeing to the minimum 60 percent time commitment to the research project for three years.

**Small Grant (R03):** These grants are intended to stimulate applications from individuals who are considering a research career in occupational safety and health; as such, the minimum time commitment is 10 percent. It is expected that a recipient would subsequently compete for a career development grant (K01) or for a traditional research project grant (R01) related to occupational safety and health. The award is not intended to supplement ongoing or other proposed research; nor is it intended to be a mechanism for providing institutional support.

The section on the small grant program has been revised to increase the level of support to \$25,000 and to allow salary support for the investigator.

The small grant investigators must be U.S. citizens or non-citizen U.S. nationals who are predoctoral students, post-doctoral researchers (within three years following completion of doctoral degree or completion of residency or public health training), and junior faculty members (no higher than assistant professor). If university or institutional policy requires that a more senior person be listed as the Principal Investigator, it should be clear in the application which person is the small grant investigator. A biographical sketch is required for the small grant investigator, the supervisor, and other key consultants, as appropriate. Except for applicants who are assistant professors, there must be one or more named mentors to assist with the project.

This non-renewable award provides support for project periods of up to two years to conduct exploratory or pilot studies, to develop or test new techniques or methods, or to analyze data previously collected. Awards will not exceed \$25,000 per year in direct costs for salary support (plus fringe benefits), technical assistance, equipment, supplies, consultant costs, domestic travel, publications, and other costs. The indirect costs will be based upon the negotiated indirect cost rate of the applicant organization. An individual may not receive more than two small grant awards, and then, only if the awards are at different stages of development (e.g., doctoral student, post-doctoral researcher, or junior faculty member).

#### RESEARCH OBJECTIVES

The NIOSH program priorities applicable to this program are occupational lung disease, musculoskeletal injuries, occupational cancers, severe occupational traumatic injuries, cardiovascular diseases, disorders of reproduction, neurotoxic disorders, noise-induced loss of hearing, dermatologic conditions, psychological disorders, control techniques, and respirator research. These priority areas represent the leading diseases and injuries related to risks on the job, and the NIOSH intends to support projects that facilitate progress in preventing such adverse effects among workers. Investigators may also apply in other areas related to occupational safety and health, but the rationale for the significance of the research to the field of occupational safety and health must be developed in the application. Potential applicants with questions concerning the acceptability of the proposed work are strongly encouraged to contact the technical information contact listed in this announcement under INQUIRIES.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF MINORITIES AND WOMEN IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

Applications must be submitted on form PHS 398 (rev. 9/91). State and local government applicants may use form PHS 5161-1 (rev. 3/89); however, form PHS 398 is preferred. Forms and the complete Program Announcement are available from the NIOSH and CDC addresses cited below. These forms are also available from institutional offices of sponsored research and from the Office of Grant Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda MD 20892, telephone (301) 496-7441.

To identify responses to this announcement, check "yes" and type "NIOSH Announcement Number OH-92-923" under item 2a of page 1 of the PHS 398 or at the top of the face page of the PHS 5161-1.

Receipt dates for new R01s and R18s are February 1, June 1, and October 1 (competing continuation deadlines are 1 month later). Receipt dates for K01s and R03s are March 1, July 1, and November 1. This is a continuous announcement, consequently, these receipt dates will be ongoing until further notice.

Applications must be received by these receipt dates to be considered in the review cycle for that date. The receipt date will be waived only in extenuating circumstances. To request such a waiver, an explanatory letter must be included with the signed completed application. No waiver will be granted prior to the receipt of the application.

The original and five copies of the PHS 398 or the original and two copies of the PHS 5161-1 application must be submitted to the address below on or before the specified receipt dates provided above:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
5333 Westbard Avenue  
Bethesda, MD 20892\*\*



Applications received under this announcement will be assigned to an Initial Review Group (IRG). The IRGs, consisting primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit. Notification of the review recommendations will be sent to the applicant after the initial review. Secondary review will be by the appropriate National Advisory Council.

#### AWARD CRITERIA

Applicants will compete for available fund with all other approved applications assigned to that ICD. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

For technical information and to request the complete program announcement, contact:

Roy M. Fleming, Sc.D.  
Associate Director for Grants  
Centers for Disease Control  
National Institute for Occupational Safety and Health  
1600 Clifton Road, NE  
Building 1, Room 3053, MS-D30  
Atlanta, GA 30333  
Telephone: (404) 639-3343

For business information:

Ms. Carole J. Tully  
Grants Management Specialist  
Grants Management Branch  
Procurement and Grants Office  
Centers for Disease Control  
Room 300, MS-E14  
255 E. Paces Ferry Road, NE  
Atlanta, GA 30305  
Telephone: (404) 842-6630

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.262. This program is authorized under the Public Health Service Act, as amended, Section 301 (42 U.S.C. 241); the Occupational Safety and Health Act of 1970, Section 20(a)(29 U.S.C. 669(a)); the Federal Mine Safety and Health Amendments Act of 1977, as amended, Section 501(30 U.S.C. 951) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52. This program is not subject to review as governed by Executive Order 12372, Intergovernmental Review of Federal Programs.

#### RESEARCH TO BETTER UNDERSTAND AND PREVENT MEASLES

NIH GUIDE, Volume 21, Number 21, June 5, 1992

PA NUMBER: PA-92-84

P.T. 34; K.W. 0715125, 1002045, 0740075, 0710070, 1002019, 0765033

National Institute of Allergy and Infectious Diseases

#### PURPOSE

Since the introduction of the measles vaccine in 1963, basic research on the measles virus has been reduced in this country. Recently, there has been a resurgence of measles in the U.S., and measles continues to be a deadly disease in the developing world. The National Institute of Allergy and Infectious Diseases invites investigator-initiated research grant applications to explore the basic biology of the measles virus and the host's response to infection. The purpose is to expand the understanding of the biologic basis of measles with the goal of developing improved vaccines to prevent disease and measles-related infant deaths. State-of-the-art application of knowledge derived from this research should lead to new vaccines with reduced primary failure rates that induce long-lasting immunity and can be given safely to very young infants. Success in this endeavor will require basic research in measles virology, immunity, genetics, and pathogenesis.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Research to Better Understand and Prevent Measles, is related to the priority area of immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report:

## ELIGIBILITY REQUIREMENTS

Research grant applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) Award.

## MECHANISMS OF SUPPORT

Applications considered appropriate responses to this announcement are the traditional research project grants (R01) and the FIRST Award (R29).

## RESEARCH OBJECTIVES

### Background

From 1981-1988, a steady average of 3,000 cases of measles occurred each year. This represents a reduction of over 99 percent from the 400,000 to 700,000 annual cases per year reported before the introduction of the measles vaccine in 1963. However, in 1989, there were 18,193 cases, and in 1990, the number rose to 27,672 cases. These cases were reported from all but one state. The 1990 outbreak year included the largest number of cases since 1977 and the largest number of deaths (89) since 1971. Of the reported cases, 22.7 percent included complications, and 21.1 percent (5844) required hospitalization. At one medical center, nine percent of the hospitalized cases eventually required intubation.

The epidemiology of the disease in the U.S. is changing, and the distribution of cases is shifting from older, previously vaccinated, school-age children to younger, unvaccinated children. As more outbreaks occur in younger children, more infants less than 1 year old are exposed.

The principal cause of the re-emergence of measles in the U.S. is the failure to vaccinate children at the appropriate age. Although very effective when used properly, the current vaccine has deficiencies as a public health tool. There is a primary failure rate of about five percent, and thus, susceptible individuals accumulate in the population. The failure rate is higher if the current vaccine is given at less than 15 months of age when maternal antibody interferes with vaccine efficacy. Measles is highly infectious and can spread even in communities where a high percentage of the population is vaccinated.

In developing countries, measles continues to be a deadly disease claiming over one and a half million deaths each year. In those countries, infants are at greatest risk for serious complications during the interval between loss of maternal antibody and receipt of vaccine. In both U.S. inner cities and inner cities abroad, this window of exposure is too wide. In order to close this window and protect young infants, new vaccines are needed that can safely overcome the maternal antibody barrier. Development of improved vaccines will depend upon new insights gleaned from basic research.

### Research Objectives and Experimental Approaches

This program announcement is intended to stimulate measles research on a broad front, with an emphasis on studies necessary for the development of improved vaccines. Research projects are sought that investigate topics including, but not limited to: the quantitative and qualitative differences between vaccine-induced and naturally induced measles immunity, the antigens required for protective humoral and cellular immunity, the development of efficient methods for delivery of immunogens, strategies to overcome maternal antibody as a block to immunization, characterization of measles immune response in young infants, the viral correlates of virulence, factors contributing to immunologically induced adverse events, and the changing epidemiology of measles. Also needed are improved laboratory methods for studying viral genetics and an animal model for measles.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions that disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.



For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the research grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit (February 1, June 1 and October 1). Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. On the first (face) page, item 2a, of the application, the word "Yes" must be checked and the title and number of the announcement typed in the space provided: PA-92-84: Research to Better Understand and Prevent Measles.

The original and five legible copies of the application must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications in response to this announcement will be assigned on the basis of established Public Health Service Referral Guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, and in accordance with the standard NIH peer review procedures. Following scientific-technical review of the applications considered to have significant and substantial merit, a secondary review will be by the appropriate national advisory council or board.

#### AWARD CRITERIA

Applications will compete for available funds with all other applications considered to have significant and substantial merit. The following will be considered when making funding decisions: relative scientific merit, program relevance, availability of funds.

#### INQUIRIES

Direct inquiries regarding programmatic issues to:

James M. Meegan, Ph.D.  
Virology Branch  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3A15  
Bethesda, MD 20892  
Telephone: (301) 496-7453  
Fax: (301) 402-0804

Direct inquiries regarding fiscal matters to:

Mr. Todd Ball  
Chief, Microbiology and Infectious Diseases GM Section  
Grants Management Branch  
Division of Extramural Affairs  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B35  
Bethesda, MD 20892  
Telephone: (301) 496-7075

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.856, Microbiology and Infectious Disease Research. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### MINORITY SCHOOL FACULTY DEVELOPMENT AWARD

NIH GUIDE, Volume 21, Number 21, June 5, 1992

PA NUMBER: PA-92-85

P.T. 44; K.W. 0720005, 0715040, 0715032, 0715165

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: July 1, 1992

Application Receipt Date: August 24, 1992

#### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) announces a program directed at developing the research capabilities of faculty investigators at minority schools in areas relevant to cardiovascular, pulmonary, and hematologic diseases and resources. The purpose of the award is to encourage the enhancement of research skills in the areas of interest to the NHLBI by faculty members at minority institutions and to increase the number of minority individuals involved in research endeavors.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Minority School Faculty Development Award, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Grants in this program will be made to domestic minority institutions on behalf of awardees, each of whom will work with a mentor at a nearby (within 100 miles) research center, who is recognized as an accomplished investigator in the research area proposed, and who will provide guidance for the awardee's development and research plan. A minority school is defined as a domestic medical or non-medical college, university or equivalent school in which students of minority ethnic groups, including Blacks, Hispanics, American Indians, and Asian and Pacific Islanders, comprise a majority or significant proportion of the school enrollment.

Candidates for this award are minority school faculty members who (1) are citizens of the United States, non-citizen nationals or permanent residents at the time of application, (2) have a doctoral degree or equivalent in a biomedical or behavioral science, (3) wish to receive specialized training in cardiovascular, pulmonary, or hematologic research, and (4) have the background and potential to benefit from the training. Each candidate must identify and complete arrangements with a nearby mentor (within approximately 100 miles), who is recognized as an accomplished investigator in the research area proposed, and who will provide guidance for the awardee's development and research plan. Plans for the intensive training during the summer period (two to three months) as well as during the academic years must be developed with the mentor.

#### MECHANISM OF SUPPORT

The mechanism of support is the Minority School Faculty Developmental Award (K14). Awards will be made to the minority institution on behalf of the awardee. Each award will have a duration of five years and is non-renewable. These awards may not be transferred to another institution or another faculty member. Funding beyond the first year of the grant is contingent upon satisfactory progress during the preceding year. If funds are to be transferred to the mentor's institution for any purpose, arrangements for the transfer or conduct of activities must be formalized in a contract or written agreement with the mentor's institution.

The awardee may receive salary support up to a maximum of \$50,000 plus fringe benefits per year for five years. All funds must be used to support the awardee. Awardees must commit 100 percent of effort during summer and/or off quarter periods

and at least 25 percent of effort during the academic year. In addition to the salary request for the candidate, support for up to 10 percent of the mentor's salary during the summer experience may also be requested. Up to \$20,000 per year will be provided for research support. Details regarding the apportionment of these funds between the minority institution and the research center must be worked out with the mentor at the research center and agreed to by representatives of both institutions. Indirect costs will be awarded on eight percent of the total direct costs exclusive of equipment. The indirect cost rate on subcontract costs for the mentor's institution may not exceed eight percent of total costs.

## RESEARCH OBJECTIVES

The Minority School Faculty Development Award is intended to:

- o Encourage the development of faculty investigators at minority schools in areas relevant to cardiovascular, pulmonary, and hematologic\* diseases and transfusion medicine.
- o Stimulate cardiovascular, pulmonary, and hematologic disease research, prevention, control, and education by offering minority school faculty members the opportunity to enhance their research capabilities in these areas.

\* Within the NHLBI, the term "hematologic" covers research on thrombosis and hemostasis, immunohematology, blood cell disorders, hematopoiesis, thalassemia, sickle cell disease, transfusion medicine including blood component and derivative therapy, blood substitutes and blood resource management, aspects of AIDS-products in AIDS prevention and treatment, and AIDS-related bone marrow and hematologic disorders. Other Institutes of the NIH are responsible for research on disorders of white cells, including the leukemias and other blood malignancies, and basic immunology related to the lymphoid system. Therefore, NHLBI cannot provide support for such studies.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research finds can be of benefits to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native American (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

## LETTER OF INTENT

Each prospective applicant is requested to forward a letter of intent that includes a descriptive title, the name and address of the research mentor, and any other participating institutions. Such letters are requested for the purposes of obtaining an indication of the number and scope of the applications to be reviewed. A letter of intent is not binding, is not a requirement of submission, and does not enter into the review of the application.

The letter of intent is requested by July 1, 1992, and is to be addressed to:



Scientific Review Administrator  
Research Training Review Committee  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 550  
Bethesda, MD 20892

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91). Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquires, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892 (telephone 301-496-7441.)

Applicants are advised to obtain the NHLBI Guidelines from the contact listed in "INQUIRIES" before preparing an application.

The title and number of the announcement must be typed in section 2a on the face page of the application.

The commitment of the institution to the faculty candidate's research and development must clearly be presented in the application. This should include statement(s) from the Dean and departmental chair indicating that the candidate will be provided with sufficient release time from other duties to accomplish the research goals stated in the application.

The completed original application and three legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Two additional copies of the application must be sent to the Scientific Review Administrator of the Research Training Review Committee listed in LETTER OF INTENT.

Applications must be received on or before August 24, 1992. Applications received after this date will be returned to the applicant without review.

#### REVIEW PROCEDURES

All applications will be reviewed for scientific and technical merit by the Research Training Review Committee of the Division of Extramural Affairs, NHLBI, followed by a second level review by the National Heart, Lung, and Blood Advisory Council.

#### AWARD CRITERIA

Applications will compete for available funds with other approved career development award applications assigned to the NHLBI. The following will be considered in making funding decisions:

- o Technical merit of the application as determined by peer review
- o Availability of funds
- o Program balance among the research areas of the announcement

#### INQUIRIES

Written and telephone inquiries are encouraged. Guidelines for this program may be obtained from any of the following:

John Fakunding, Ph.D.  
Division of Heart and Vascular Diseases  
National Heart, Lung and Blood Institute  
Federal Building, Room 3C04  
Bethesda, MD 20892  
Telephone: (301) 496-1724

Helena Mishoe, Ph.D.  
Division of Blood Diseases and Resources  
National Heart, Lung and Blood Institute  
Federal Building, Room 504  
Bethesda, MD 20892  
Telephone: (301) 496-6931

Mary Reilly, M.S.  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 640A  
Bethesda, MD 20892  
Telephone: (301) 496-7668

Jane Davis  
Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A15C  
Bethesda, MD 20892  
Telephone: (301) 496-7257

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.837, 93.838, and 93.839. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816

# NIH GUIDE

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## For Grants and Contracts

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**Printing & Reproduction Branch**  
**National Institutes of Health Room B4BN23,**  
**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 22  
June 12, 1992

RICHARD W HURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000



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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

## NOTICES

### INFORMATION AND CLARIFICATION OF REVISED APPLICATION FORM PHS 398 and PHS 2590

NIH GUIDE, Volume 21, Number 22, June 12, 1992

P.T. 34; K.W. 1014006

National Institutes of Health

The purpose of this notice is to clarify questions raised by NIH staff and the research community about modifications and changes in the revised forms PHS 398 and PHS 2590 (rev. 9/91).

The application for continuation of a Public Health Service Grant, form PHS 2590, is now available for use. The last receipt date for the use of previous forms PHS 398 (rev. 10/88) and 2590 (rev. 10/88) will be October 1, 1992.

#### RECEIPT DATE

The NIH guidelines governing receipt dates for applications have not changed and may be found on page 4-14 of the PHS Grants Policy Statement (rev. 9/91). Item 2 in the first full paragraph in the instructions on page 8 of the revised PHS 398 application is applicable to PHS agencies and programs that do not utilize the NIH Division of Research Grants.

Receipt date guidelines are as follows:

"For grant applications processed through the NIH's Division of Research Grants, the Division of Research Grants (DRG) system requires that applications must be RECEIVED by the published application receipt dates. However, an application received after the deadline may be acceptable if it carries a legible proof-of-mailing date assigned by the carrier and the proof-of-mailing date is not later than 1 week prior to the deadline date."

#### TYPE SIZE

Some fonts designated by the manufacturer as 10-point fonts do not meet the application requirement of 1/8 inch in height for capital letters. Therefore, it is suggested that, when using a 10-point font, the height should be measured with a standard device for measuring type size. If a particular font does not clearly meet the requirement, use of a larger font is recommended.

#### PAGE LIMITATIONS

The page limit for the Research Plan (exclusive of the publications in the Progress Report) has been increased from 20 to 25 pages. There is now a three-page limit on the Introduction and a six-page limit on literature cited. Please note that each literature citation must now include TITLES as well as all authors, book or journal, volume number, page numbers, and year of publication.

Items such as background graphs, diagrams, tables, and charts, previously included in the Appendix, now must be incorporated in the Research Plan.

#### APPENDIX

There are important changes in the guidelines for Appendix material. Page 24 of the PHS 398 (rev. 9/91) contains instructions regarding the Appendix.

The Appendix may now contain 10 publications or manuscripts SUBMITTED or accepted for publication. Supplementary background graphs, diagrams, tables, and charts directly pertinent to the application may NOT be submitted as appendix material.

The Appendix is not to be used to circumvent the page limitations in the Research Plan. Only publications, manuscripts, questionnaires, photographs of electron micrographs, gels, or other materials that do not copy well should be included in the Appendix. Because secondary reviewers do not get copies of the Appendix, a photocopy of any photographs in the Appendix, MUST also be included in the Research Plan. Photocopies must be large enough to be legible to reviewers.

Letters regarding consultants and collaborators must be included in Section 7 of the application, not in the Appendix. See page CC, Table of Contents.

ANY APPLICATION THAT DOES NOT ADHERE TO TYPE SIZE, PAGE LIMITATION, OR APPENDIX GUIDELINES WILL BE RETURNED TO THE APPLICANT, WITHOUT REVIEW, FOR REVISION AND RESUBMISSION FOR A SUBSEQUENT APPLICATION RECEIPT DATE.

## FORMATS AND FACSIMILE COPIES

Facsimile copies of forms are acceptable provided they closely resemble the original application. Spacing on forms other than the face page may differ slightly from the actual form. Contact Dr. Patricia Straat, Deputy Chief for Referral, DRG, telephone (301) 496-7447, to check acceptability of facsimiles.

The Other Support and the Personnel sections are formats, not forms. The information presented for these two formats does not have to look like the format nor does the exact wording on the page have to be included. Thus, for example, all key personnel who have no other support may be listed on a single page with Other Support as the heading, their names typed in and "none" indicated after "active" and "pending."

DO NOT send in a separate page of Other Support on the format in the application for each person listed for whom "none" is checked.

## DESCRIPTION/ABSTRACT - FORM PAGE 2

The information provided in the Description is sent to the National Technical Information Service (NTIS) and is available to the public. Therefore, proprietary information should not be included here as it may affect potentially patentable inventions.

## PERSONNEL

The NIH is interested in tracking individuals on research projects, especially graduate students, to determine whether or not they subsequently pursue careers in research. Birth dates are needed to track these individuals. (The birth dates of key personnel were previously requested on the Biographical Sketch page of the application kit.)

o Which individuals should be listed at the bottom of Form Page 2 where it asks for "Personnel Engaged on Project?"

The instructions (page 16) for Form Page 2 state that those individuals who will participate in the SCIENTIFIC EXECUTION of the project, including collaborating investigators, individuals in training (who are employees on the project), and support staff must be listed. In most instances, support staff need not be reported since they rarely participate in the scientific execution of the project. Thus, dishwashers, secretaries, animal caretakers, and most technicians need not be listed here, but should be included on the budget page.

o Summary of Personnel Listings

Other Support Page - Key Personnel

Personnel Form Page 2 - Key Personnel plus individuals in research training who are employees on the project

Budget Page - All personnel who are employees of the applicant organization

o Are dates of birth required or optional?

For the reasons stated above, whenever possible, dates of birth should be included for key personnel and graduate students.

o In the Form PHS 2590, which individuals should be listed for personnel in the progress report on Form Page 7?

The same categories of individuals listed on Form Page 2 of the PHS 398 application must be listed here. Thus, current and planned key personnel plus individuals in training who are employees on the project must be listed.

## BUDGET PAGE

o What is the definition of a full-time appointment?

NIH staff recognize that full-time appointments may be different in terms of actual months per year or days per week at the applicant organization. Therefore, the definition of a full-time appointment must be in accordance with the institutional policy and used consistently by each institution on all Federal grant applications. Anything less than full-time, in accordance with the organization's policy, should be identified with an asterisk.

In cases such as the Veterans Administration, where the type of appointment cannot be identified by months, an asterisk should be placed in the column and a full explanation provided under Justification.



o What is institutional base salary?

The definition of institutional base salary on Page 17 has not changed and is the annual compensation that the applicant organization pays for the individual's appointment, whether that individual's time is spent on research, teaching, patient care, or other activities. For example, a physician's clinical salary that is paid by the applicant organization under its standard payroll system is considered part of the institutional base salary.

o Should actual or projected institutional base salary be used in salary calculations?

The institution must list the salary in effect at the time of submission. However, if, for instance, a known state-wide or institution-wide salary or other increase, such as promotion or merit pay, has been approved or is projected, salaries based on that figure may be requested provided the anticipated increase is explained in the Justification section.

o Should the institutional base salary be listed when it is greater than \$125,000?

When an institutional base salary exceeds the salary limitation, the higher salary should be listed. The salary limitation, currently \$125,000, is an annual requirement that is subject to change with each appropriation. The salary requested, however, cannot be awarded at a rate in excess of \$125,000 per year.

o What should be listed in the institutional base salary category if, for instance, a graduate student is paid hourly and does not have an institutional base salary?

An asterisk must be placed in the column for base salary and an explanation must be provided under "Justification" to explain the basis for the salary requested.

o Why is institutional base salary required for the continuation application, form PHS 2590, and optional for the competing application, form PHS 398?

Institutional base salary is optional because those applications are available to outside reviewers. However, institutional base salary will be requested by the grants management staff if the application is funded.

Since the information on the PHS 2590 is reviewed by NIH staff, not by outside reviewers, and the information is needed by grants managers, institutional base salary is required for the continuation application.

#### BIOGRAPHICAL SKETCH

If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

#### OTHER SUPPORT

Other Support information is critical for determining effort and resources available to the Principal Investigator for that project. Overlapping support or over commitment of effort determinations are part of the stewardship roles of NIH program and grants management staff.

The format on form Page 7 was designed as a guide to ensure that all of the pertinent information is included. Other Support should not be more than one page per key personnel per other support source. Specific aims of the other projects, for example, should be condensed into about five lines.

o What is institutional support?

Institutional support includes funds or resources paid for or provided by the institution for personnel, trainees, and/or equipment that has not been reported elsewhere in the application.

o What resources should be listed for Other Support?

All funds and resources, whether Federal, non-Federal or institutional, available to the Principal Investigator/program director in direct support of the research endeavors through research or training grants, cooperative agreements, contracts, fellowships, and endowed chairs must be listed on the Other Support page. Research endeavors relate to an investigator's entire program of research. However, in the case of prizes and gifts, only those that support the specific projects must be reported in Other Support.

While most gifts are monetary, other non-monetary gifts, such as equipment, must be reported when used in direct support of the project and not reported elsewhere in the application.

o What is meant by dates and costs of the entire project?

The dates of the entire project should reflect only the currently active award for the Other Support, e.g., the current competitive segment. Both direct and indirect costs must be listed here as well as for the Other Support for the current year.

#### CHECKLIST

For Misconduct in Science, new institutions must report the date of Initial Assurance. Institutions that have submitted Annual Reports must list the date of the most recent submission.

The checklist must be the last page on ALL copies of the application.

Certification/assurance of a Drug-Free Workplace is applicable for new or revised applications (Type 1). It is NOT required in applications for competing and noncompeting continuations (Type 2 and Type 5).

Applicants applying for a non-competing continuation must have filed forms for Civil Rights, Handicapped Individuals, Sex Discrimination, and Age Discrimination in order to have received a competing award. Therefore, applicants should mark "FILED" for these assurances on the checklist for the PHS 2590.

#### SUBJECTS ENROLLED IN STUDIES

o In form PHS 2590, the Application for Continuation, what information should be included in the table for reporting subject data on form Page 7?

Use the table on form Page 7 to provide the number of male and female subjects within each category enrolled in the study to date, that is, cumulatively since the most recent competitive award.

#### EDITORIAL CLARIFICATIONS

On page 9 of the form PHS 398, the page limitations chart describing the Research Plan should read "Sections 1-4" instead of "Sections A-D."

#### INSTITUTIONAL NATIONAL RESEARCH SERVICE AWARDS (NRSA)

Indirect costs under Institutional NRSA's, other than those awarded to State and local government agencies, will be reimbursed according to the PHS Grants Policy Statement (rev. 9/91), which states eight percent of total allowable direct costs exclusive of tuition and related fees and expenditures for equipment or AT THE ACTUAL INDIRECT COSTS RATE, WHICHEVER RESULTS IN A LOWER DOLLAR AMOUNT. (The capitalized portion was inadvertently omitted from the new application forms.)

#### RESEARCH CAREER DEVELOPMENT AWARDS - - - APPENDIX

The Appendix material instructions should have reflected the new guidelines for the Appendix for individual research grant applications. Thus, no more than six publications and manuscripts submitted or accepted for publication may be submitted with NEW applications.

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### SCREENING FOR AGENTS AGAINST THE HUMAN IMMUNODEFICIENCY VIRUS

NIH GUIDE, Volume 21, Number 22, June 12, 1992

RFP AVAILABLE: NCI-CM-37818-28

P.T. 34; K.W. 0715008, 0755060, 0740012, 0780015

National Cancer Institute

The National Cancer Institute (NCI), Division of Cancer Treatment, Developmental Therapeutics Program, Antiviral Evaluations Branch, is seeking an organization to provide assistance in the primary screening of experimental agents utilizing the HTLV/LAV (human AIDS virus). An organization is sought that will supply the necessary equipment, personnel, and facilities to conduct screening on the scale of 20,000 tests per year. The tasks will include maintaining and expanding one or more cell lines and the virus necessary to infect these cells, the preparation of experimental agents for testing, and the collection and submission of data. The project will primarily involve cell culture, although approximately 20 percent of the work will involve in vitro detailed agent testing, and less than 10 percent of the work will involve in vivo testing with murine leukemia virus.

It is anticipated that one cost-reimbursement contract, completion form, will be awarded as a result of the solicitation. This contract is planned to be incrementally funded over a five-year period. The proposed contract project represents a recompetition of Southern Research Institute, N01-CM-87237.

Because of the nature of work involving live human immunodeficiency virus (HIV), offerors must show evidence at the time of the best and final offer that P-3 level biocontainment facilities are available for use on this project.

This project requires that the following restriction be applied. "The NCI signs legally binding agreements with certain suppliers (often pharmaceutical or chemical companies) that state that all information on compounds submitted by the supplier will be held confidential. The successful offeror will be expected to test such commercially confidential (discreet) agents. The NCI believes that the compound cannot be sent to potential competitors of the supplier, and thus pharmaceutical and chemical companies must be excluded from the competition. For purposes of this exclusion, a pharmaceutical or chemical company is defined as an organization that manufactures and/or sells drugs and chemicals to the general public for profit."

All responsible sources may submit a proposal that shall be considered by the NCI. This announcement is not a Request for Proposals (RFP). RFP No. NCI-CM-37818-28 will be available on or about June 12, 1992, with a response date of July 27, 1992, for the receipt of proposals. All copies of the RFP may be obtained by written request to:

Ms. Carolyn Barker  
Contract Specialist, Research Contracts Branch  
Treatment Contracts Section  
Executive Plaza South, Room 603  
9000 Rockville Pike  
Bethesda, MD 20892

No collect calls will be accepted.

#### INTERNATIONAL COOPERATIVE BIODIVERSITY GROUPS

NIH GUIDE, Volume 21, Number 22, June 12, 1992

RFA AVAILABLE: TW-92-01

P.T. 34; K.W. 1002000, 0730000, 0715035, 0715040, 0715125, 0715129

National Institutes of Health  
National Institute of Mental Health  
National Science Foundation  
U.S. Agency for International Development

Letter of Intent Receipt Date: September 1, 1992

Application Receipt Date: November 17, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACTS NAMED IN "INQUIRIES" BELOW.

#### PURPOSE

The National Institutes of Health (NIH), the National Institute of Mental Health (NIMH), the National Science Foundation (NSF), and the U.S. Agency for International Development (USAID), (hereafter "the Government" or "the Participating Agencies") invite applications for the establishment of "International Cooperative Biodiversity Groups (ICBGs)." The purpose of these Groups will be to address the interdependent issues of biodiversity conservation, sustained economic growth, and human health in terms of drug discovery for cancer, infectious diseases including AIDS, cardiovascular diseases, mental disorders, and diseases of primary concern to developing countries.

Under this program, the NIH will be allocated funds pursuant to their respective authorizing statutes from the NIMH, NSF, and USAID. The Fogarty International Center (FIC) of the NIH will administer this program.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, International Cooperative Biodiversity Groups, is related to the priority needs of several diseases of interest to the NIH.



Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Public and private non-profit institutions, Governments and their agencies, and foreign institutions are eligible to participate. Applicant institutions must be in the United States or in a participating developing country. For-profit institutions may participate as members of the Group.

#### MECHANISM OF SUPPORT

Awards will be made as cooperative agreements (U01). Assistance via cooperative agreement differs from grant awards in that sponsoring Government components anticipate substantial programmatic involvement in the project.

A Group, under a single Group Leader (Principal Investigator), is expected to be a consortium of Associate Programs working together to form a multidisciplinary and/or multi-institutional team from academic, non-profit, and/or commercial organizations. At least one of the Group's Associate Programs must be located in a developing country. Although not required, it is likely that one or more U.S. institutions will play a key role.

Interaction of academic and non-profit research institutions with commercial (including industrial) organizations and the sponsoring Government agencies will favor development of novel approaches to drug development, biodiversity conservation, and sustained economic growth. Active participation of the private sector is encouraged. Interaction of academic and non-profit institutions with industry and Government will encourage the creation of innovative, interdisciplinary approaches.

#### FUNDS AVAILABLE

The Government anticipates making three awards (cooperative agreements) for project periods of three to five years, contingent upon the availability of funds. Approximately \$1.5 million (total costs) for first-year funding has been set aside. Cost effectiveness of program design in relation to proposed budgets is an important funding criterion.

#### RESEARCH OBJECTIVES

The goals of the ICBG Program are to:

- o Discover, isolate, and evaluate, preclinically, agents from natural sources to treat and prevent cancer, infectious diseases including Acquired Immunodeficiency Syndrome (AIDS), cardiovascular diseases, mental disorders, and other diseases and medical conditions of primary concern to developing countries.
- o Undertake inventories of biological diversity and develop collection practices compatible with conserving biodiversity and produce documentation of all collected material.
- o Support research training targeted toward the needs of developing or other countries represented within the Group and related to the scope of the RFA, and to augment field experience and training of U.S. scientists in areas unique to the developing country. Research training supported through an appointment related to this award may take place in-country or in the U.S. and may be degree-earning. Training costs and plans, including letters of commitment from institutions where training is to be conducted, must be specified in the application.
- o Assist in improving the scientific infrastructure within participating developing country(ies) where the biodiversity resources are found. This could include assistance for herbaria, museums, and laboratories, supply of necessary equipment in these facilities, and enhancement of collecting and screening capabilities, and intellectual property management in the host country.

Applications should stress creative, synergistic, and multidisciplinary approaches, with substantial developing country participation, to biodiversity conservation, drug development, and sustainable economic growth.

#### SPECIAL REQUIREMENTS

Applicants should emphasize, among other factors, developing country participation and collaboration.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

NIH and ADAMHA policy is that applicants for grants and cooperative agreements to conduct any research involving human subjects or human materials be required to include minorities and women in study populations such that

research findings can be of benefit to all persons at risk of the disease, disorder or condition under study.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by September 1, 1992, a letter of intent including a descriptive title of the proposed project, a description of the intended components, and to the extent known, names of members of the proposed ICBG (Group Leader and Associate Programs) and their institutions. The letter of intent, which helps in planning for the review, does not commit the sender to submit an application, nor is it required for submission of applications.

The letter of intent is to be sent to:

Dr. Sherry Dupere  
Scientific Review Administrator  
Fogarty International Center  
National Institutes of Health  
Building 31, Room B2C32  
Bethesda, MD 20892  
Telephone: (301) 496-2516  
FAX: (301) 402-2056

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for this grant. These forms are available from sponsored research offices at most institutions and from the Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

The deadline for receipt of applications is November 17, 1992. APPLICATIONS RECEIVED AFTER THIS DATE WILL BE RETURNED WITHOUT REVIEW.

#### REVIEW CONSIDERATIONS

Applications will be received by NIH Division of Research Grants (DRG) and reviewed by the DRG and FIC for completeness. Incomplete applications will be returned to the applicant without further review.

The FIC will evaluate applications for responsiveness to determine if they meet the goals and objectives of the program as described in this RFA. Applications judged to be non-responsive will be administratively withdrawn, and the proposed Group Leader and institutional official will be notified.

The Government may conduct an initial peer review to eliminate applications clearly not competitive for award. The Government will withdraw from further competition those applications judged to be noncompetitive and notify the Group Leader and institutional official. Those applications judged both competitive and responsive will be further evaluated, using the review criteria in the RFA for scientific and technical merit by a peer review group convened by the NIH. Subsequent review will be provided by the FIC Advisory Board. Based on recommendations from the peer review process, the Participating Agencies will recommend funding levels and priorities. Final funding decisions will be made by the Director, FIC.

#### INQUIRIES

It is strongly advised that prospective applicants contact the FIC early in the planning process to discuss prospective applications and to obtain supplemental clarifying information and instructions including information about a briefing for prospective applicants in June or July that may be developed. It is essential that prospective applicants receive a copy of the RFA from the FIC before applying.

Direct written and telephone inquiries concerning the RFA to:

Dr. Kenneth Bridbord  
Chief, International Studies Branch  
Fogarty International Center  
National Institutes of Health  
Building 31, Room B2C32  
Bethesda, MD 20892  
Telephone: (301) 496-2516

Direct inquiries regarding fiscal matters to:

Mrs. Silvia Mandes  
Grants Management Officer  
Fogarty International Center  
National Institutes of Health  
Building 31, Room B2C39  
Bethesda, MD 20892  
Telephone: (301) 496-1653

Questions related to the review of applications may be directed to Dr. Sherry Dupere at the address and telephone number indicated in LETTER OF INTENT.

#### AUTHORITY AND REGULATIONS

Awards under this program are made under authorization of the Public Health Service Act, Sections 301, 307, and 482, 42 U.S.C. 241, 242l and 287b and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. The participation by other agencies in funding the program is authorized under the Economy Act (31 U.S.C. 1535).

#### AFTER-SCHOOL CARE AND ITS EFFECTS ON THE DEVELOPMENT OF CHILDREN

NIH GUIDE, Volume 21, Number 22, June 12, 1992

RFA AVAILABLE: HD-93-02

P.T. 34, AA; K.W. 0404000, 0417000, 0730005, 0730010, 0404004

National Institute of Child Health and Human Development

Application Receipt Date: August 24, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Human Learning and Behavior Branch (HLB) of the Center for Research for Mothers and Children (CRMC) and the Demographic and Behavioral Sciences Branch (DBS) of the Center for Population Research (CPR), both of the National Institute of Child Health and Human Development (NICHD), are inviting grant applications for the support of research on after-school care and its effects on the development of children.

The purpose of the RFA is to encourage innovative and highly qualified researchers in the areas of social and behavioral sciences to study (a) the after-school arrangements for school-age children who vary in terms of gender, race, and socio-economic background and (b) the impact of these arrangements on the development of children. The research needs to take into account are (a) the after-school environments, including self-care arrangements, (b) the demographic and psychological characteristics of the families who choose the care arrangements, (c) the characteristics of the communities from which children come, and (d) the characteristics of the children who are placed in the different after-school care arrangements.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, After-School Care and Its Effects on the Development of Children, is encouraging research that has implications for the social and psychological well being of children and their families. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of States and local government and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.



## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

## FUNDS AVAILABLE

\$600,000 are set aside for the first year of support of total costs for the entire program. It is anticipated that four grants will be made.

The level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NICHD, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

### Background

More than 65 percent of women with school-aged children are employed out of the home, and this figure is expected to increase to 75 percent by 1995. At present, research-based information on the quality of after-school care of school-age children of employed mothers is sparse and inconclusive. In the absence of such information, the regulation of quality in such programs is based on studies of preschool-age children. This leads to ambiguous and inappropriate requirements. The systematic investigation of the conditions of after-school care and the impact on the many children involved is timely and has important scientific and policy implications.

### Objectives

The RFA encourages social and behavioral scientists to study unresolved questions pertaining to after-school care. There are several areas that need to be researched. For example:

- o Stability of care over the years and its effects on the development of children. Stability is conceptualized as the extent to which children stay in the same care arrangements and the extent to which the providers within an arrangement stay the same.
- o Cumulative effects of care as contrasted with concurrent effects. It is important to find out the extent to which observed effects of care depend (a) on characteristics of the care the child receives at the time the child is being examined and/or (b) on the cumulative impact of months or years of after-school care of known quality and extent.
- o The role of the community, the family, and child characteristics as mediators of the effects of after-school care on the development of children. Communities and families vary in the resources they have at their disposal. Families vary in their coping skills, and children vary in their health, disposition, and ability to take advantage of resources. All these are expected to mediate the effects of after-school care on the development of children.
- o The experiences of children in the different after-school care arrangements and how these impact on the development of children. Children's outcome may be influenced by (a) opportunities for interactions with peers and adults, (b) opportunities for autonomy and choice, (c) potentially harmful or dangerous experiences, and (d) their own satisfaction with after-school care.

Children's outcome can be evaluated in different domains of functioning. For example, one could evaluate the children in terms of school performance, performance on intelligence tests, self-esteem, social adjustment as measured by relations within the family and among peers, engagement in antisocial behavior such as disruptive behavior in school, or exhibiting aggressive behavior.

It is expected that the proposed research will include descriptive studies, and studies designed to test hypotheses about after-school care and its effects on the development of children.

## SPECIAL REQUIREMENTS

Investigators are encouraged to request funds to travel once each year to meet with the other investigators who are funded through this RFA. The meetings will be held at the NIH, Bethesda, MD. The purpose of the meetings is to have investigators working in the same general area share information about research methods and findings.

## STUDY POPULATIONS

The research subjects will be boys and girls between the ages of 6 and 12 and their families. Investigators are encouraged to study male and female children and families varying in their racial and socio-emotional background. NIH policy requires research grants to include minorities and women, so that research findings can be of benefit to all. If women and minorities are excluded or inadequately represented in the proposed research, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed by the research design and mentioned in form PHS 398 in Sections 1-4 of the Research Plan and summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations. Should the study focus on a single minority population, a rationale should be provided.

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in responding to this RFA. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Applications must be received by August 26, 1992. If an application is received after that date, it will be returned to the applicant without review.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NICHD staff will return the application to the applicant. The applicant will then have the option of submitting it to the DRG for review in competition with unsolicited applications at the next review cycle.

Applications may be triaged by an NICHD peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will undergo further scientific merit review. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by a special peer review committee convened by the NICHD. The second level of review will be provided by the National Advisory Child Health and Human Development Council.

The review criteria are:

- o scientific and technical significance and originality of proposed research;
- o appropriateness and adequacy of the approach and methodology proposed to carry out the research;
- o qualifications and research experience of the Principal Investigator, collaborating investigators and staff, particularly, but not exclusively, in the area of the proposed research;
- o experience of the Principal Investigator and collaborating investigators in conducting research with school-age children and with minority research participants, if such participants are included;
- o availability of resources necessary to perform the research, including ability to recruit and maintain data collectors;
- o appropriateness of the proposed budget and duration in relation to the proposed research.

## AWARD CRITERIA

The anticipated date of award is April 1, 1993.

Responsiveness to the RFA, scientific merit, and technical proficiency, as described in the application, will be the predominant criteria for determining funding.

## INQUIRIES

Potential applicants are welcome to ask for clarification of issues and questions concerning this RFA.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Hildegard P. Topper, M.S.  
Special Assistant, Office of the Director  
National Institute of Child Health and Human Development  
Building 31, Room 2A04  
Bethesda, MD 20892  
Telephone: (301) 496-0104

Direct inquiries regarding fiscal matters to:

Edgar D. Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-1303

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.865, Research for Mothers and Children. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health System Agency review.

## NORMATIVE BEHAVIORAL RESEARCH ON ETHNIC MINORITIES

NIH GUIDE, Volume 21, Number 22, June 12, 1992

RFA AVAILABLE: HD-93-03

P.T. 34, FF; K.W. 0404000, 0413001, 0404004, 0414005

National Institute of Child Health and Human Development  
National Institute of Mental Health

Application Receipt Date: August 26, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANT MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

## PURPOSE

The purpose of this RFA is to generate high-quality behavioral research about the NORMATIVE developmental experiences, processes, and outcomes of minority children in the U.S.A.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority goals. This RFA, Normative Behavioral Research on Ethnic Minorities, is related to this initiative since it will stimulate research about variations in psychological health among minority children and about the familial, cultural, and societal conditions that influence such variations. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone (202) 783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. It is suggested that applicants have research



experience pertinent to the research agenda described in the RFA.

#### MECHANISM OF SUPPORT

This RFA will use the individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

#### FUNDS AVAILABLE

The NICHD has set aside \$800,000 for the first year of support for the entire program. It is anticipated that five awards will be made. The NIMH will set aside \$300,000 for the first year of support (total costs) of the program, and it is anticipated that two awards will be made. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NICHD and NIMH, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The purpose of this RFA is to stimulate behavioral research about the normative development of minority children living in the U.S. Minority children constitute a rapidly growing segment of the population and the documentation of their normative development and conditions that influence it are of scientific importance.

This RFA calls for research that is driven by ecological and cultural models of human development, showing how variations in communities and their institutions, family characteristics, parental lifecourse experiences, parental attitudes and behaviors, economic resources, and social support systems affect the development of minority children. Consequently, the RFA encourages interdisciplinary research by psychologists in collaboration with demographers and/or sociologists and/or economists and/or anthropologists.

The developmental outcomes that need to be investigated are in all domains of human functioning, but special emphasis is needed in the areas of social and emotional development.

This RFA encourages research that considers variations in the medical health and nutritional status of minority children. These variations in health and nutritional status need to be documented and related to the environmental factors and to the outcome of minority children's development.

The research agenda for studying the normative development of minority children is extensive. No single research project to be supported through this RFA is expected to address all of the research issues or to utilize all of the perspectives suggested by the above description of purpose.

#### SPECIAL REQUIREMENTS

To help investigators who are funded through this RFA to share information and to learn from each other, it is recommended that each applicant ask for funds to attend an annual meeting of the grantees. The meeting will take place at the NIH, Bethesda, MD.

#### STUDY POPULATIONS

The RFA calls for research on all minority children. These include African American, Asian American, Native American, Pacific Islanders, and Hispanic children. Research on children of all ages (0 to 17) is welcome. Newborns, infants, toddlers, preschool age children, and school-age children of all ages and both sexes, including adolescents, may be the subjects of research applications to be submitted in response to this RFA.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in responding to this RFA. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies of the application must also be sent to:

Dr. Laurance Johnston  
Division of Scientific Review  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Bethesda, MD 20892\*\*  
Telephone: (301) 496-1485

Applications must be received by August 26, 1992. If an application is received after that date, it will be returned to the applicant without review. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NICHD staff will return the application to the applicant. The applicant will then have the option of submitting it to the Division of Research Grants for review in competition with unsolicited applications at the next review cycle.

Applications may be triaged by a standing peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will undergo further scientific merit review. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by an appropriate peer review group convened by the NICHD (after consultation with NIMH staff). The second level of review will be provided by the Councils of NICHD and NIMH. The review criteria for this RFA are listed below.

- o scientific significance, technical excellence, and originality of proposed research;
- o appropriateness and adequacy of the approach and methodology proposed to carry out the research;
- o qualifications and research experience of the Principal Investigator, collaborating investigators and staff, particularly, but not exclusively, in the area of the proposed research;
- o experience of the Principal Investigator and collaborating investigators in conducting research with minority research participants;
- o availability of resources necessary to perform the research, including ability to recruit and maintain minority data collectors;
- o appropriateness of the proposed budget and duration in relation to the proposed research.

#### INQUIRIES

Potential applicants are welcome to ask for clarification of issues and questions concerning this RFA.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Hildegard P. Topper, M.S.  
Special Assistant, Office of the Director  
National Institute of Child Health and Human Development  
Building 31, Room 2A04  
Bethesda, MD 20892  
Telephone: (301) 496-0104

or

Mary Ellen Oliveri, Ph.D.  
Chief, Personality and Social Processes Research Branch Division of Basic Brain and Behavioral Science  
National Institute of Mental Health  
5600 Fishers Lane, Room 11C-10  
Rockville, MD 20857  
Telephone: (301) 443-3566

Direct inquiries regarding fiscal matters to:

Edgar D. Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
6130 Executive Boulevard  
Executive Plaza North, Room 505 G  
Bethesda, MD 20892  
Telephone: (301) 496-1303

or

Bruce Ringler  
Chief, Grants Management Branch  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C15  
Rockville, MD 20857  
Telephone: (301) 443-3065

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.865, research for Mothers and Children, and 93.242, Mental Health Research Projects. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. Awards are also under authorization of PHS Act, Title V, Part B. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health System Agency review.

#### HUMAN FETAL TISSUE BANKS

NIH GUIDE, Volume 21, Number 22, June 12, 1992

RFA AVAILABLE: HD-92-10

P.T. 34; K.W. 0780020, 0705035, 0780030

National Institute of Child Health and Human Development  
Letter of Intent Receipt Date: June 26, 1992  
Application Receipt Date: August 3, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The purpose of this RFA is to support the initial research necessary to provide and assess the quality and quantity of human fetal tissues available solely from spontaneous abortions and ectopic pregnancies to serve as sources for transplantation therapy; to develop and test effective methods for human fetal tissue banks to use in obtaining, testing, culturing, and preserving those tissues and transporting them for transplantation; and to gain information on the epidemiology and mechanisms of early pregnancy loss. Transplantation therapy requires viable, sterile, well-characterized tissue that is obtained, maintained, and distributed to investigators under conditions of highest quality control. Data generated from the studies supported under this RFA to develop the initial stages of human fetal tissue banks will be evaluated and utilized in the establishment of a national network of human fetal tissue banks entirely dependent on tissue from spontaneous abortions and ectopic pregnancies.



## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Human Fetal Tissue Banks, is related to the priority area of maternal and infant health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1), through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, both public and private, such as universities, colleges, hospitals, laboratories and units of state or local governments. Applications from minority individuals and women are encouraged.

### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Resource-Related Research Project Grant (R24). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed two years for Phase I of this study. The anticipated award date is September 28, 1992.

This announcement is for a single competition and the application receipt deadline is August 3, 1992. Once it is established that there are sufficient data from the Phase I studies to support development of a network of defined fetal tissue banks, additional applications will be solicited and competed.

### FUNDS AVAILABLE

It is anticipated that up to six grants will be awarded under this program, contingent upon receipt of a sufficient number of meritorious applications and the availability of funds. For these awards, \$3,000,000 for total costs in the first year have been set aside.

### RESEARCH OBJECTIVES

The use of fetal tissue transplants has been advocated for several years as a means of alleviating symptoms of a number of devastating diseases. Fetal tissue transplants may allow replacement of tissues and cell products that have been damaged, destroyed or that never developed properly due to disease or a genetic disorder.

Using fetal tissues from spontaneous abortions and ectopic pregnancies only, tissue banks are to be developed to determine the ability of such facilities to provide adequate amounts of the biological materials required to further fetal tissue research and to establish protocols, tissue processing innovations, logistical systems, and a data base appropriate to the need.

For a detailed description of the research objectives, please request a copy of the full RFA from the contact person named below.

### SPECIAL REQUIREMENTS

Data obtained from the Phase I study of fetal tissue banks, dependent on tissue exclusively from spontaneous abortions and ectopic pregnancies, will be evaluated at the end of the first year by a panel of outside experts convened by, and advisory to, the NICHD. Based on the recommendations of the advisory panel, plans for Phase II will be developed.

It is expected that at least two meetings of the awardees, NICHD staff, and the advisory panel consultants, during both the first and subsequent years, will be required to assess progress and workscope. These meetings will be of benefit to the grantees and will allow them to address unforeseen difficulties, assist in establishing networking of fetal tissue banks and to assess the schedule of progress. Funds for this travel should be requested in the application.

### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF MINORITIES IN CLINICAL RESEARCH STUDIES

Applicants are requested to collect and study tissues from all spontaneous abortions and ectopic pregnancies derived from women admitted to the participating hospitals for treatment of these conditions during the duration of the study. Tissues that are lost from the study should be accounted for to provide needed epidemiologic data.

It is NIH and ADAMHA policy that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study; special emphasis should be placed on the need for inclusion of minorities in studies of diseases, disorders, and conditions that disproportionately affect them. If minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of racial/ethnic group. In addition, racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, 1-4 of the Research Plan and summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). For further information about this policy, see the RFA.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by June 26, 1992, a letter of intent that includes a descriptive title of the proposed research; the name, address, and telephone number of the Principal Investigator; the identities of other key personnel and participating institutions; and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NICHD staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent should be sent to:

Delbert H. Dayton, M.D.  
Genetics and Teratology Branch  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Executive Plaza North, Room 643  
Bethesda, MD 20892  
Telephone: (301) 496-5541  
FAX: (301) 402-2085

#### APPLICATION PROCEDURES

The receipt date for applications is August 3, 1992. The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at appropriate institutional offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, MD 20892, telephone (301) 496-7441.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of an application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box checked.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, exact photocopies, in one package to:

DIVISION OF RESEARCH GRANTS  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies of the application must also be sent to:

Laurance Johnston, Ph.D.  
Acting Director, Division of Scientific Review  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Executive Plaza North, Room 520  
Bethesda, MD 20892

## REVIEW CONSIDERATIONS

Applications will be received by the NIH Division of Research Grants and reviewed for completeness. Incomplete applications will be returned to the applicant. NICHD staff will review the applications for responsiveness to the RFA. Applications judged to be nonresponsive will be returned. Responsive applications may be subjected to a triage by a peer-review group to determine their scientific merit relative to the other applications received in response to this RFA. NICHD will withdraw from competition those applications judged to be noncompetitive and notify the applicant and institutional official. Those applications judged to be competitive will be further evaluated for scientific/technical merit by a review group convened solely for this purpose by the Division of Scientific Review, NICHD. (For specific review criteria, see full RFA). Following review by the Initial Review Group, applications will be evaluated by the NICHD Advisory Council for program relevance and policy issues before awards for meritorious applications are made.

## AWARD CRITERIA

Applications must be of sufficiently high merit, based on the review criteria, to warrant funding. Geographic location of approved projects will also be a consideration.

## INQUIRIES

Written and telephone inquiries concerning this RFA are welcome.

Direct inquiries regarding programmatic issues to:

Delbert H. Dayton, M.D.  
Chief, Genetics and Teratology Branch  
Center for Research for Mothers and Children  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 643  
Bethesda, MD 20892  
Telephone: (301) 496-5541

Direct inquiries regarding fiscal matters to:

Ms. Mary Ellen Colvin  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 501  
Bethesda, MD 20892  
Telephone: (301) 496-1303

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.865, Research for Mothers and Children. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC241), and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or review by a Health Systems Agency.



## ONGOING PROGRAM ANNOUNCEMENTS

### MAGNETIC RESONANCE SPECTROSCOPY AND CANCER TREATMENT

NIH GUIDE, Volume 21, Number 20, May 29, 1992

PA NUMBER: PA-92-86

P.T. 34; K.W. 0715035, 0706030

National Cancer Institute

#### PURPOSE

The National Cancer Institute (NCI), through the Diagnostic Imaging Research Branch (DIRB) of the Radiation Research Program, seeks grant applications through Interactive Research Project Grants (IRPGs) in order to establish multidisciplinary research in the area of early detection and prediction of tumor response to treatment using magnetic resonance imaging (MRI)-guided magnetic resonance spectroscopy (MRS).

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Magnetic Resonance Spectroscopy and Cancer Treatment, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

It is intended that this program will be supported through the interactive R01 mechanism. Elements of the program may be supported as individual R01 grants. The NCI seeks to encourage the coordinated submission of related research project grant applications from investigators who want to collaborate on a common cancer research theme, but do not require extensive shared physical resources or core functions. A minimum of three independent investigators with related research objectives are encouraged to submit concurrent, collaborative, cross-referenced individual research project grant applications (R01) that share a common research focus. Applications may be from either a single institution or a consortium of institutions. Applications will be reviewed independently for scientific merit. Meritorious applications will be considered for funding both as independent awards and in the context of the overall proposed collaboration.

Applicants will be responsible for the planning, direction, and execution of the proposed projects. One Principal Investigator out of the group MUST be identified as the "Program Coordinator," and must be cited in all applications on page 2 of form PHS 398. Individual investigators may request funds for the time and effort contributed toward the coordination of the overall research and for collaborative resource activities.

Additional information about the interactive R01 mechanism may be found in the NIH Guide for Grants and Contracts, January 10, 1992, in PA-92-29, "Interactive Research Project Grants for Cancer."

Awards will be administered in accordance with Public Health Service Policy as described in the PHS Grant Policy Statement, DHHS. Publication No. (OASH) 90-50,000 revised October 1, 1990.

#### RESEARCH OBJECTIVES

##### Background Information

Conventional, or proton, MRI provides predominantly anatomic information, whereas MRS is essentially an in vivo assay of tissue biochemistry. Recently, it has become possible to integrate MRS with routine MRI, so that local abnormalities detected by MRI can be examined biochemically by MRS before and after therapeutic interventions. In contrast to currently available imaging methodologies, which rely predominantly on changes in tumor size to evaluate therapeutic response, MRS can detect early biochemical changes in tumor composition that precede morphologic changes in response to therapeutic interventions. Studies in animal tumors have

provided strong evidence that MRS can readily observe the effects of therapies on tumor metabolism. However, it is not entirely clear if MRS could be used in humans for prediction of therapeutic outcome or as a guide for treatment planning. At present, few clinical studies have been done in this area. More work is required to determine if the changes seen in animal tumor models are evident in their human counterparts and, if so, to investigate the underlying biologic mechanisms. The focus of the proposed research is to examine proton MRI-guided localized MRS as a tool for early detection and prediction of tumor response to treatment.

The clinical application of MRS in oncology is in its early stages of development. The majority of clinical MRS studies to date have been performed in a limited number of patients. In spite of the technical limitations imposed on early clinical studies, the preliminary phosphorus-31 MRS results indicate that changes in pH, PME, and PDE levels may be predictive of response to radiation and chemotherapy. Moreover, preliminary proton MRS studies in humans indicate the differences in the levels of choline, N-acetyl aspartate, and, in some instances, lactate or alanine both between tumor and normal brain and within tumors. The developments of the MRS methodology and technology have progressed considerably in the areas of spatial localization, spectral editing, data analysis, quantitation, and data presentation. At a recent NCI workshop, an expert panel identified the need for carefully planned clinical studies.

The goal of this initiative is to conduct well-focused, prospective clinical studies using currently available, routinely applicable, methodology to begin comprehensive testing of the potential for 31P MRS to predict and/or detect therapeutic response in patients with tumors. Given the limited resources available at any one institution and the effort required to perform repeated measurements in each patient for response predictor studies, it seems prudent to coordinate such studies among several institutions. The critical issue in these studies is quality control, i.e., setting precise standards for performance and interpretation of spectroscopic studies.

#### Research Goals and Scope

This new program announcement will stimulate the scientific community to research, in a centrally coordinated fashion, the utility of MRI-guided MRS for early detection and prediction of therapeutic response in patients with tumors. A consensus-based development of the experimental design will include data acquisition, presentation and processing (e.g., standards of MRS performance, well-defined technical requirements, and method(s) of spectral localization, quantification, and data analysis).

This announcement seeks to encourage the following research topics in proton MRI-guided MRS in preclinical and clinical cancer research:

- o Detection and prediction of immediate treatment response
- o Prediction of final outcome
- o Evaluation of the direct effect of drugs
- o Differentiation of viable tumor from treatment-induced necrosis, edema, and scar

It is also expected that the proposed studies will address the following needs:

- o In vivo metabolic characterization of human tumors
- o Correlation of metabolic characteristics with histological features (e.g., tissue types, tumor grade)
- o Correlation of metabolic characteristics with clinical and biological behavior (growth rate, degree of differentiation, probability of recurrence, metastatic potential)

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in

developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in the Research Plan, 1-4, AND summarized in 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for this program announcement. These forms are available at most institutional business offices, the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441, and the NCI program director named below.

The PA number and title must be typed on line 2a of the face page of the application form.

The use of the IRPG mechanism must be mentioned briefly in form PHS 398, Sections 1-4 of the Research Plan. The goal of the collaborative efforts MUST be identified in the specific aims of each application, with the major rationale and explanation for the use of the IRPG mechanism to be given in Section 7, Consultants/Collaborators. A complete list of applications in the IRPG must be provided in Section 7, as well as an indication of the specific collaborations to be established for the individual application under consideration.

Requests for limited shared resources, if any, must be proportionally budgeted in each application based on anticipated use, with a full explanation given in the budget. Personnel Time and Effort requests for management of shared resources are allowable. If consortium arrangements between independent institutions are proposed that would make transfer of funds for required new equipment impractical, the entire equipment request may be budgeted by the responsible laboratory. This must be clearly justified. All PHS and NIH grants policies will apply to applications received in response to this announcement.

If the applicant has an approved assurance covering the research (multiple project assurance for human subjects/full assurance of compliance for animal subjects), the applicant should provide with the application certification of institutional review board (IRB) approval, if humans are involved, and verification of the institutional animal care and use committee (IACUC) approval, if animals are involved. These reviews and approvals should occur PRIOR TO SUBMISSION of the applications for award and the certifications and verifications should be SUBMITTED WITH the applications. Failure to provide required certifications and verifications within applications could result in deferral or rejection of the application. If animals or humans will be subjects of research at PERFORMANCE SITES OTHER THAN THE APPLICANT ORGANIZATION, the applicants must identify, with the application, the assurance status of each participant. Failure to provide this information within applications may result in deferral or rejection.

Submit a signed, typewritten original of the application, including the Checklist, and five signed, exact



photocopies, in one package to the address below. The photocopies must be clear and single sided.

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Those applications judged to be complete will be further evaluated for scientific and technical merit by study sections of the DRG. Following the scientific and technical review, the applications will receive a second level of review by NIH staff who consider the application in light of the special needs of the Institute.

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the customary NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate national advisory council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this program announcement and inquiries about whether or not specific proposed research would be responsive are encouraged and should be directed to:

Faina Shtern, M.D.  
Chief, Diagnostic Imaging Research Branch  
Radiation Research Program  
National Cancer Institute  
Executive Plaza North, Suite 800  
Bethesda, MD 20892  
Telephone: (301) 496-9531

Dr. Shtern welcomes the opportunity to clarify any issues or questions from potential applicants.

Direct inquiries regarding budgetary/administrative issues to:

Joan Metcalfe  
Grants Management Specialist  
Grants Administrative Branch  
National Cancer Institute  
Executive Plaza South, Room 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800, extension 28

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.395, Cancer Treatment Research. Awards are made under the authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816



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# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 23  
June 26, 1992

RICHARD W. MURRY

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\*\*51350E\*\*

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GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

## NOTICES

### GERIATRICS PROGRAM

NIH GUIDE, Volume 21, Number 23, June 26, 1992

P.T. 34; K.W. 0710010, 1014006

National Institute on Aging

As part of a continuing effort to build and sustain a broad program of research on diseases of older persons and the underlying pathophysiologies, the Geriatrics Program (GP) of the National Institute on Aging encourages investigators to submit applications that propose moderate budgets and durations. GP staff continues to encourage research on aging and physical function and performance, endocrinology, osteoporosis, arthritis, cardiovascular issues, nutrition, metabolism, and related aging research areas. Studies on etiology and pathophysiology of age-related disorders, as well as clinical studies, are encouraged.

### INQUIRIES

GP staff can supply more information about this notice and about the ongoing program initiatives.

Written inquiries may be addressed to:

Geriatrics Program  
National Institute on Aging  
Gateway Building, Suite 3E327  
Bethesda, MD 20892

Telephone inquiries may be made to Ms. Vivian Williams, telephone (301) 496-6761, who will direct the inquiries to the appropriate staff person.



NOTE: This is a reprint of the announcement as it appeared in the Federal Register on June 25, 1992.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Cooperative Agreements for Demonstration Projects for Capacity Building at Historically Black Colleges and Universities (HBCUs)

ACTION: Notice of availability of funds and request for applications.

This demonstration program is to assess whether or not an infrastructure responsible for the administration of sponsored programs will enable HBCU institutions to increase their participation in Federal and private sector health related scientific, technical, and service activities and thereby improve their capacity to conduct such activities.

AUTHORITY: Applications are being accepted under the authority of section 301 of the Public Health Service Act.

AVAILABILITY OF FUNDS: It is anticipated that at least three projects will be funded for an estimated cost of up to \$250,000 (indirect and direct costs) per 12-month budget period for a four year project period. There is approximately \$750,000 available for funding this program in fiscal year 1992.

ELIGIBILITY CRITERIA: Eligibility is limited to HBCUs as defined by the U.S. Department of Education that offer, at a minimum, a Baccalaureate Degree. Priority will be given to HBCUs that have some experience seeking and receiving Federal funding but do not have a formal office responsible for administering sponsored programs.

OBJECTIVES: To determine whether or not the capacity of HBCUs to conduct scientific, technical, and service related activities can be improved through infrastructure support of an office for sponsored programs.

BACKGROUND: In Executive Order 12677 on Historically Black Colleges and Universities, President Bush outlined his objectives with HBCUs as being to advance the development of human potential, to strengthen the capacity of HBCUs to provide quality education, and to increase opportunities to participate and benefit from Federal programs. In keeping with the intent of the Executive Order, the Public Health Service (PHS) has developed this demonstration activity.

In discussions with representatives of HBCU institutions, both administrators and Principal Investigators (PIs) and Federal staff involved in HBCU activities, it has been hypothesized that HBCUs would be better able to achieve the objectives outlined by the President if their institutional infrastructure included support for sponsored program activities.

This support, which has been labeled an office of sponsored programs, would assist in developing each institution's ability to obtain and maintain sponsored program activities, i.e., public and private sector supported-research, training, evaluation, and services grants and contracts. In turn, this would improve the institution's capacity to participate further in Federally sponsored programs aimed at scientific, technological, and service-related activities and improve the quality of their educational programs by providing students with access to research activities and staff who are involved in the conduct of such activities.

This activity is one that requires the commitment of all key staff at the institution. Therefore, those institutions interested in participating in this activity will need to document the commitment of the chief operating and academic officers and the organization that represents the institution's faculty to support this activity.

The institution will also need to provide a commitment to establish and operate a sponsored programs office at a level within the institution that will permit it to carry out the responsibilities set forth below.

The office would:

- (a) serve as the key advisor to institutional officials in the identification and development of institutional capabilities in scientific, technical, and service delivery activities;
- (b) be responsible for the pre and post award activities related to the application for, and the administration of grants and contracts;
- (c) assist the institution's staff in developing their writing skills and ability to develop applications for support;
- (d) identify and assist key administrators to develop institutional policy to conform with Federal and other sponsor requirements;
- (e) identify new and innovative methods of obtaining support for institutional activities;
- (f) assist in the development of applications including writing a narrative, preparation of a proposed budget, provision of support documents and certifications such as Civil Rights requirements, animal use, and human subjects research;
- (g) participate in the development of indirect cost rates and audit activities;
- (h) follow up on applications and serve as a continuing interface between the institution and the funding organization;
- (i) assist the PI in applications that are approved but not funded, returned, or disapproved, to determine what the

- weaknesses and how best they might be overcome through preparation of a revised application for resubmission;
- (j) assist the PI so that the resources required, e.g., space, personnel, release time, to conduct a funded project are obtained in a timely manner;
  - (k) monitor the activities on the supported projects to ensure that (1) appropriate progress is being made on the sponsored projects, (2) problems are being dealt with, and (3) funding agencies are being contacted when appropriate;
  - (l) assure that all reporting requirements are adhered to by the institution and the PI, including financial status reports and programmatic reports.

In addition to the usual technical assistance, the Federal Government will provide additional substantive programmatic technical assistance which requires that this program be a cooperative agreement.

On-site technical assistance will be provided by Federal contractors who have demonstrated expertise in the field of sponsored programs at other educational institutions. This will include assistance in the development of office systems and information resources including materials, data systems, internal publications, staff surveys of capabilities and interests, and methods of dealing with the internal dynamics of an institution of higher education.

In addition, the Federal Government will provide the staff from the recipient institutions with a general orientation program to PHS sponsored activities at each PHS agency. This will acquaint the recipients with PHS organizations, programs, policies, procedures, and contacts for further information.

Recipients will be required to develop a method of evaluating the success of the new office activities at their institution. This should include input from faculty and administration.

**HEALTHY PEOPLE OBJECTIVES:** The Public Health Service urges applicants to submit work plans that address specific objectives of "Healthy People 2000." Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

**USE OF GRANT FUNDS:** The grant will provide, at a minimum, funds for one full-time professional and one support staff person. In addition, institutions may provide staff and resources at no cost to the grant. In order not to delay this demonstration project, the professional staff person must be employed at the institution, or committed to be an employee at the institution at the time of award (on or before September 30, 1992), have knowledge of the institution's programmatic capabilities, and have some working acquaintance with the administration of Federal grants and/or contracts. No funds will be available under this program for alterations and/or renovations.

**FEDERAL INVOLVEMENT:** Listed below are the activities for which the Federal employees will be substantially involved in this project:

- 1) Federal employees and/or contractors will provide on-site assistance in the establishment of internal systems and procedures for a sponsored program office.
- 2) The Federal government will provide a general orientation session on Federal programs and grant and contract policies and procedures.

**APPLICATION NARRATIVE:** The narrative should contain the following information, addressed in the same order as in this announcement.

- 1) A statement describing the need for an office of sponsored programs at the institution. This should include the institution's assessment of their current activities and capabilities and how the project would improve their capacity to obtain funding and improve the quality of the institution's education of its students.
- 2) A listing of sponsored activities conducted by the institution over the past three years giving a synopsis of the activity, annual dollar amount, and source of support.
- 3) A listing of the current staff used to identify sources of funding, assist in application development and implementation.
- 4) A written commitment from the institution's President/Chief Academic Officer and the organization that represents the institution's faculty that they will support the development of this office and use it for identification of sources of support and assistance in obtaining and retaining support.
- 5) A description of the facilities, support services, and resources to be available for this project.
- 6) A description of start up activities and institutional support activities for the new office.
- 7) A description of how this office will be organized and work on a daily basis.
- 8) A statement as to if and how the institution will support the continuation of the activity once Federal funding ends.
- 9) A clearly detailed list of project goals, objectives, and milestones for the entire project.
- 10) A plan to collect data and other information to evaluate whether or not the goals and objectives are met, including baseline and comparative data, baseline sources, duration, amount, and supported activities.
- 11) A detailed budget narrative must be included with cost justifications.
- 12) A copy of the curriculum vitae of professional staff for the project must be included.

**APPLICATION REVIEW PROCESS:** Applications will be reviewed for technical merit by an objective review panel comprised of qualified Federal reviewers. Incomplete and/or applications that are nonresponsive to the program announcement will be returned to the applicant without further consideration.

**REVIEW CRITERIA:** Applications will be reviewed and evaluated on the following criteria:

- 1) The extent to which the applicant's goals and milestones meet the objectives of the program.
- 2) The level of institutional commitment on the part of the faculty and the administrative staff toward the establishment and operation of the office.
- 3) The degree to which an organization has a capability that can be stimulated by this project.
- 4) The extent to which professional staff involved in this project are qualified to accomplish the project objectives and their knowledge of the institution's infrastructure and operating procedures.
- 5) The applicant's view of what constitutes an office of sponsored programs, the actual location of the office, including organizational chart, and how the office will function within the institution.
- 6) The extent to which the organization is committed to continuing support for this project once Federal funding terminates.
- 7) The degree to which the evaluation plan will be able to measure achievement of the objective and the quality of the methods to be used.
- 8) The extent to which the budget is cost-effective and appropriate to the scope and objectives of the project.

Funding decisions will be based on the recommendations of the objective reviewers. Final funding decisions will be made by the Director, Office of Management, Office of the Assistant Secretary for Health, Public Health Service.

**LETTER OF INTENT:** HBCUs planning to submit an application for a cooperative agreement under this program announcement are asked to submit a letter of intent by June 23, 1992. The letter of intent should be sent to Mr. Theodore J. Roumel, Chief, Grants Policy Branch, Division of Grants and Contracts, ORM/OM, Room 17A45, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857. Such notification will be used for review and planning purposes. The letter of intent is voluntary and the fact that an HBCU does not elect to submit a letter of intent does not preclude an HBCU from applying.

**APPLICATION FORM:** The standard application form PHS 5161 (3/89) must be used for this program and applicants must submit a signed original and two copies of the complete application. Application kits can be obtained from and completed applications submitted to the Grants Management Officer, Office of Minority Health, Office of the Assistant Secretary for Health, Suite 1102, Rockwall II Building, 5515 Security Lane, Rockville, MD 20852. Applicants should not request Federal funds that exceed the stipulated budgetary limit.

**INFORMATION CONTACTS:** Questions regarding programmatic information should be directed to: Ms. Nina Darling, Grants Policy Branch, Division of Grants and Contracts, ORM/OM, Office of the Assistant Secretary for Health, Room 17A45, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857, telephone (301) 443-1874. Questions regarding business management aspects should be directed to Ms. Carolyn Williams, Office of Minority Health, Suite 1102 Rockwall II Building, 5515 Security Lane, Rockville, MD 20852, telephone (301) 227-8758.

**APPLICATION DEADLINE:** The application deadline is July 22, 1992, and applications shall be considered as meeting the deadline if they are either:

- (1) Received on or before the deadline date, or
- (2) Postmarked on or before the deadline date and received in time for submission to the independent review group. A legibly dated receipt from a commercial carrier or U.S. Postal service will be accepted in lieu of postmark. Private metered postmarks shall not be acceptable as proof of timely mailing.

Late applications will not be accepted for processing and will be returned to the applicant.

This program is not subject to State review under E.O. 12372, "Intergovernmental Review of Federal Program."

There is no Catalog of Federal Domestic Assistance Number for this program since it is viewed as a one time project.

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### U.S. TRIAL OF ACCELLULAR PERTUSSIS VACCINE

NIH GUIDE, Volume 21, Number 24, June 26, 1992

RFP AVAILABLE: NICHD-OD-92-16

P.T. 34; K.W. 0740075, 0755015

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) is planning a clinical safety trial using a DTP vaccine in which the pertussis component is the acellular pertussis toxoid developed by NICHD scientists. An efficacy trial of this DTP is currently underway in Goteborg, Sweden.

The safety trial is to begin in January 1993. The study will include three lots of the investigational DTP vaccine



(the products of three separate manufacturing runs) and one lot of commercial whole-cell DTP. These vaccines will be randomly labelled A, B, C, and D and will be bottled in single-dose vials. Each lot of vaccine will be sufficient to immunize 1,000 infants at 2, 4, and 6 months of age.

In summary, 4,000 infants will be immunized, with 1,000 each receiving either vaccine A, B, C, or D. The entire process will be completed for each child within a period of four months. The offeror must be able to recruit and immunize at least 1,000 infants (ideally the offeror could recruit and immunize all 4,000) over the time period of the resulting 12 months. The offeror will be expected to randomly identify a 10 percent sample of infants to be bled for antibody measurements. One-third of the selected infants will be bled one month after the first injection, one-third one month after the second injection, and one-third one month after the third injection. In addition, blood samples will be taken from a five percent randomly identified group of infants before the first injection at two months of age. All blood samples will be stored as frozen serum (4x4) and shipped frozen to the NICHD as directed by the Project Officer. The NICHD will be responsible for serological analyses.

This announcement is a new solicitation. The issuance of this Request for Proposals (RFP) will be on or about June 26, 1992, and proposals are due by 4:00 p.m. (local time), August 27, 1992. The Institute plans to award one to four contracts, depending on the number of recruits that the successful offerors plan to select. Those organizations desiring a copy of the above RFP may send written requests to:

Mrs. Lynn Salo  
Office of Grants and Contracts  
Contract Management Branch  
National Institute of Child Health and Human Development  
6100 Executive Blvd., Room 7A07A  
9000 Rockville Pike  
Bethesda, MD 20892

All requests must cite the RFP number above and include two self-addressed mailing labels. All sources who consider themselves qualified are encouraged to submit a proposal.

This advertisement does not commit the Government to make an award.

#### NATIONAL RESEARCH SERVICE AWARD - INSTITUTIONAL TRAINING APPLICATIONS

NIH GUIDE, Volume 21, Number 23, June 26, 1992

RFA AVAILABLE: DE-92-05

P.T. 44; K.W. 0720005, 0715148, 0785055

National Institute of Dental Research

Letter of Intent Receipt Date: August 10, 1992  
Application Receipt Date: September 10, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute of Dental Research (NIDR) invites applications proposing institutional training programs in basic and clinical sciences pertaining to: (1) oral biology and (2) epidemiology. Applications in other areas of oral health research are also acceptable. Proposed training must be relevant to the goals of the NIDR, as described in the NIDR Long-Range Research Plan for the Nineties, "Broadening the Scope". Availability of this publication is described under INQUIRIES.

The primary objective of these training programs is to develop highly qualified clinical investigators by supporting postdoctoral training of individuals with D.D.S., D.M.D., or equivalent clinical degrees, who are committed to a career in oral health research. Applications may also include pre- and postdoctoral training for basic scientists and/or short-term training for dental students in the proposed programs.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, NRSA - Institutional Training Applications, is related to the priority area of oral health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted from domestic public and private institutions.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) National Research Service Award (NRSA) Institutional Research Training Grant (T32). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed five years; however, awards are renewable.



## FUNDS AVAILABLE

The NIDR expects to make one or two institutional training awards in response to this RFA. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIDR, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## PROGRAM CHARACTERISTICS

The training program must provide opportunities for individuals to carry out supervised biomedical or behavioral oral health research and to develop research skills. Clinical programs must have strong relationships with basic scientists that will assure dentists the opportunity to acquire the necessary foundation for future independent research.

Applications will be accepted to provide training at one or more of the following levels, given in priority order: (1) dentists pursuing a Ph.D. or equivalent degree in basic science; (2) dentists pursuing postdoctoral research training; (3) baccalaureate degree holders pursuing a Ph.D. or equivalent degree; (4) Ph.D. degree holders pursuing postdoctoral research training; and (5) pre-dental degree students pursuing a short-term research experience, usually during, but not limited to, the summer months.

For other than short-term training, preference for post-doctoral appointments must be given to individuals who have received, as of the beginning of an appointment, a D.D.S., D.M.D., or equivalent dental degree from an accredited domestic or foreign institution. Certification by an authorized official of the degree-granting institution that all degree requirements have been met is acceptable.

## LETTER OF INTENT

Prospective applicants are asked to submit, by August 10, 1992, a letter of intent that includes a descriptive title of the proposed research training program, the name, address, and telephone number of the Program Director, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDR staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Thomas M. Valega, Ph.D.  
Special Assistant for Manpower Development and Training  
Extramural Programs  
National Institute of Dental Research  
Westwood Building, Room 510  
Bethesda, MD 20892  
Telephone: (301) 496-6324  
FAX: (301) 496-4180

## APPLICATION PROCEDURES

It is strongly recommended that prospective applicants contact program staff early in the planning phase of application preparation. Such contact may help ensure that applications are responsive to this RFA.

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for this grant. Application forms are available at most institutional business or grants office, from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441, and from the NIDR program administrator named above.

This RFA is for a single competition. Applications must be received by September 10, 1992. If an application is received after that date it will be returned to the applicant without review.

## REVIEW CONSIDERATIONS

Applications will be evaluated for scientific and technical merit by the NIDR Special Grants Review Committee (SGRC), a standing NIH initial review group. Applicant interviews or site visits may be involved.

Secondary review will be by the National Advisory Dental Research Council. Among the information the Council considers will be the report of the SGRC on the plans for, and success in, recruitment of women and individuals from underrepresented minority groups.

Applications will be processed according to the following schedule:

Application Receipt Date	Initial Review Group Meeting	Council Meeting	Earliest Award Date
Sep 10, 1992	Feb/Mar 1993	May/Jun 1993	Jul 1993

## AWARD CRITERIA

The earliest award date will be July 1, 1993.

The NIDR will notify the applicant of the Council's action shortly after its meeting. Funding decisions will be made

based on the SGRC and Council recommendation, the need for research personnel in specified program areas, and the availability of funds.

The NIDR appreciates the value of complementary funding from other public and private sources, including foundations and industrial concerns, for activities that will complement and expand those supported by the NIDR.

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to Dr. Thomas M. Valega at the address indicated in LETTER OF INTENT.

Direct inquiries regarding fiscal matters to:

Theresa Ringler  
Grants Management Officer  
Extramural Programs  
National Institute of Dental Research  
Westwood Building, Room 518  
Bethesda, MD 20892  
Telephone: (301) 496-7437

Copies of the NIDR Long-Range Research Plan for the Nineties, "Broadening the Scope," are available by written request to NIDR, P.O. Box 54793, Washington, DC 20032

AUTHORITY AND REGULATIONS

NRSA Institutional Research Training Grants are made under the authority of Section 487 of the Public Health Service (PHS) Act as amended (42 USC 288). Title 42 of the Code of Federal Regulations, Part 66, is applicable to this program. This program is also described in the Catalog of Federal Domestic Assistance No. 93.121. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### MOLECULAR INTERVENTIONS FOR ENVIRONMENTALLY INDUCED DISEASE PREVENTION

NIH GUIDE, Volume 21, Number 24, June 26, 1992

RFA AVAILABLE: ES-92-03

P.T. 34; K.W. 0725005, 1007009, 0760003

National Institute of Environmental Health Sciences

Application Receipt Date: November 24, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

This RFA is the first of an anticipated series of solicitations in a broad research strategy to develop interventions at the molecular level for diseases with an environmental etiology. The current announcement focuses on the development and use of biomarkers to assess the effectiveness of intervention strategies.

The elimination of toxic agents from the environment has dominated the field of prevention. Although the causes of certain human diseases are known, explicit preventive strategies still cannot be offered for avoidance of numerous risk factors associated with many types of disease sequelae. This is because there are unavoidable risk factors and inherent biostatistical and epidemiological limitations involved in the identification and interpretation of complex disease processes and potential low-risk hazards. Recently, control strategies involving a more mechanistic approach derived from chemical and biological research have received more emphasis. The objective of the strategy is eventual intervention through preventive/protection or other active means of modulating the risk factors.

The National Institute of Environmental Health Sciences (NIEHS) has posed as one of its major goals of the 1990s the development of an effectual knowledge base that would equip clinicians to effectively treat people who are affected adversely by exposure to environmental agents. Accordingly, the NIEHS announces the availability of funds to support research efforts aimed at the development and clinical use of methods to prevent, modulate, or treat environmentally induced toxic effects. Such studies should provide new insight into the molecular bases for intervention to prevent or ameliorate environmentally induced diseases as well as associated alterations of biological processes related to toxicant exposures. The focus of this particular RFA is development and use of appropriate biomarkers to study effectiveness of potential intervention methods.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Molecular Interventions for Environmentally Induced Disease Prevention, is related to the priority area of environmental health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone (202) 783-3238.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private,

such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. Foreign applicants are not eligible for the First Independent Research Support and Transition (FIRST) Award.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01) and the FIRST Award (R29). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

#### FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for the entire program is \$1.5 million. The expected number of awards is 8-12.

This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIEHS, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The ultimate goal and scope of this research program is the support of studies that will advance knowledge to diminish the risk of disease development. There are potentially many approaches that may have application to clinical solutions to ameliorate environmental toxicant effects and/or to intercede in disease pathways.

The focus of this RFA is on the development and use of biomarkers to assess the effectiveness of intervention studies. Biomarkers, as indicators of molecular and cellular events in biological systems, may allow epidemiologists and other health professionals to better examine the relationships between environmental hazards and human health effects.

Studies should address the relationship of a biomarker to a disease process, i.e., does exposure lead to effect. As such, it is critical to link molecular intervention studies with related epidemiology studies. Further, the NIEHS is interested primarily in biomarkers correlated with non-cancer endpoints. Although applications related to cancer endpoints are acceptable, they will be weighted for programmatic balance.

The scope of these studies may range from prevention of internal exposure to the toxic agent, to treatment of effects at the cellular and molecular level, to genetic control of the disease-regulating and controlling events. Studies should be innovative, providing new insight into the molecular basis of biomarker induction and the concomitant modulation: (1) the molecular identification and quantification of exposure to environmental agents; (2) the amelioration of environmental agent-induced biological perturbations; and (3) the linkage of an environmental agent exposure to a specific disease or disease process.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

Applications must be received by November 24, 1992.

The RFA label available in the PHS 398 (rev. 9/91) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the application including the checklist, and three signed, photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIEHS staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.



The subject of this RFA may overlap with interests of other Institutes, Centers, and Divisions (ICDs). Applications will, therefore, be assigned according to extant PHS Referral Guidelines. If developing programs deal with clinical populations, applicants might wish to consider utilization of General Clinical Research Center (GCRC) facilities. More information on the GCRC program can be obtained from Dr. Judith Vaitukaitis at the National Center for Research Resources, telephone (301) 496-6595.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

William A. Suk, Ph.D., M.P.H.  
Program Administrator, Scientific Programs Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-0797

Direct inquiries regarding fiscal matters to:

Mr. David L. Mineo  
Grants Management Officer, Grants Management Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-1373

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.113 and 93.115. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 43 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### CLINICAL AND EPIDEMIOLOGIC RESEARCH ON SYSTEMIC LUPUS ERYTHEMATOSUS IN CARIBBEAN POPULATIONS

NIH GUIDE, Volume 21, Number 23, June 26, 1992

PA NUMBER: PA-92-87

P.T. 34; K.W. 0715015, 0785055, 0785035

National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Fogarty International Center

#### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases and the Fogarty International Center invite investigator-initiated grant applications and supplemental applications to explore hypotheses concerning the etiology, pathogenesis, treatment, and prevention of systemic lupus erythematosus (SLE) in Caribbean populations. The NIAID also has interest in research projects on the subject of systemic lupus erythematosus. The customary referral guidelines will apply. Applications meeting NIAID referral criteria may be assigned to that institute. Research proposed in response to this announcement may involve clinical, epidemiologic, genetic, or behavioral studies. In addition to SLE, studies of other rheumatic diseases in these populations will be considered.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Clinical and Epidemiologic Research on Systemic Lupus Erythematosus in Caribbean and African Populations, is related to the priority area of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-0325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Research grant applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as institutions of higher education, research institutions, units of State and local government and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. U.S. and foreign investigators are encouraged to collaborate. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) Award (R29).



Applications considered appropriate responses to this announcement are the traditional research project grant (R01) and the FIRST Award (R29). In addition, the Fogarty International Research Collaboration Award (FIRCA) funding mechanism may be used by NIH grantees from the U.S. to collaborate with foreign investigators. Joint efforts between U.S. and Caribbean investigators are strongly encouraged.

## RESEARCH OBJECTIVES

### Background

SLE, a chronic inflammatory disease, appears to result from an immunoregulatory disturbance brought about by the interplay of genetic, hormonal, and environmental factors. During the past three decades, SLE has emerged worldwide as a major rheumatic disease. There is a marked female predominance, with most series reporting a 9:1 female-to-male ratio and an even higher ratio during the childbearing years. Systemic lupus erythematosus appears to be more common in certain racial groups, particularly blacks. Racial differences have also been reported in the natural history and clinical manifestations of SLE.

### Research Objectives and Experimental Approaches

Studies of the general population at risk for SLE and other diseases, as well as on patient populations who have been diagnosed as having the diseases, will be accepted. The research focus may be on clinical, genetic, epidemiologic, or behavioral studies. Subject matter to be encouraged include:

- o Clinical research oriented to the cellular, organ, or human level
- o Clinical trials as well as projects to develop outcome assessment tools to define the impact of different medical approaches
- o Studies to quantify the side effects of new therapies and identify subpopulations of patients who are at increased risk for serious adverse reactions to treatment
- o Genetic studies, including studies associating susceptibility and clinical subsets with genetic markers
- o Cross-sectional as well as longitudinal epidemiologic studies
- o Studies of the natural history of lupus as well as case-control studies
- o Studies of migrant populations in the U.S. versus those remaining in their country of origin and urban/rural comparisons
- o Studies examining the impact of comorbid conditions, behavioral, environmental, and socioeconomic factors are encouraged

### STUDY POPULATIONS

The Caribbean islands are particularly well-suited for studies of systemic lupus and other diseases that disproportionately affect individuals of African descent. Each island has a substantial minority population. Among the more populated islands, Jamaica has a current population of 2.4 million, 76.3 percent are of African descent. Trinidad and Tobago have a population of 1.3 million with 43 percent African and 40 percent East Indian descent. Africans comprise 80 percent of the Barbados population. Certain diseases, such as lupus, which is known to be more frequent in African-American populations than in Caucasians, can be more readily studied on islands where it may be feasible to attain complete ascertainment of cases. On the Caribbean islands a small number of specialists see patients with certain diagnoses, thus facilitating identification and follow-up of cases. Also, most of the care is provided by a small number of medical institutions.

While new research projects are desired, applications based on current studies are also encouraged.

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

This policy applies to all studies submitted under this program announcement. The usual NIH policies concerning research on human subjects also apply. For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided. Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application. All applications are required to address these policies. NIH funding components will not award grants that do not comply with these policies.

#### APPLICATION PROCEDURES

Applicants are to use the research project application form PHS 398 (rev. 9/91) that is available at the applicant's institutional research office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. To expedite the application's routing, check the box on the application face sheet indicating that the application is in response to this announcement and type (next to the box) "Clinical and Epidemiologic Research on Systemic Lupus Erythematosus in Caribbean Populations, PA-92-87." The National Institute of Allergy and Infectious Diseases (NIAID) also has interest in research projects on the subject of systemic lupus erythematosus. Normal referral guidelines will apply, and applications meeting NIAID referral criteria may be assigned to that institute.

The application (with five copies) must be mailed to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Receipt dates for new Research Project Grants, FIRST Awards and FIRCA applications are February 1, June 1, and October 1 of each year.

#### REVIEW CONSIDERATIONS

R01 and R29 applications will be reviewed for scientific and technical merit by an appropriate Initial Review Group of the Division of Research Grants. FIRCA applications will be reviewed by a Fogarty International Center initial review group. Secondary review will be by the assigned National Advisory Council. Applications compete on the basis of scientific merit.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that institute, center, or division. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Direct inquiries regarding programmatic issues to:

Ms. Reva C. Lawrence  
Epidemiology/Data Systems Program Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Building 31, Room 4C-13  
Bethesda, MD 20892  
Telephone: (301) 496-0434

Direct inquiries regarding fiscal matters to:

Ms. Diane M. Watson  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 732-A  
Bethesda, MD 20892  
Telephone: (301) 402-3352

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## MEDICAL DEMOGRAPHY OF DEMENTIAS OF AGING

NIH GUIDE, Volume 21, Number 24, June 26, 1992

PA NUMBER: PA-92-88

P.T. 34; K.W. 0715180, 0413001, 0408006, 0730000

National Institute on Aging

### PURPOSE

The Rising Prevalence of Dementias: The dementias associated with aging are caused by more than 70 disorders and diseases; Alzheimer's disease (AD) alone is estimated to account for 60 to 70 percent and to be the major cause of institutionalization among the oldest old. The precise causes and variable courses are under intensive investigation (e.g., program announcement (PA), The Epidemiology of Alzheimer's Disease and Other Dementing Disorders of Older Age, NIH Guide Vol. 15, No. 18). But the multidimensional impact of AD and other cognitive impairments of aging ---on economic and social resources, as a cause of social dislocations, and on society in general--- is only belatedly gaining attention, and is a focus of this PA.

The incidence and prevalence of these dementias and cognitive impairments of aging are determined both by the underlying etiology of the disease and the processes that define the size and composition of the at-risk population. At the same time, AD itself is a significant determinant of other demographic patterns among the aged, e.g., living arrangements, household composition, extent of institutionalization, health care expenditures, and intergenerational transfers (economic and service). Changing demographic patterns among younger adult cohorts, on the other hand, will condition the nature and extent of resources available for caretaking and caregiving. (See PA, "Alzheimer's Disease and Related Disorders: Issues in Caregiving" NIH Guide for Grants and Contracts, Vol. 18, No. 6, February 24, 1989.)

Medical demography is the application of demographic concepts, models, and techniques to the analysis of the dynamics of morbidity and mortality at all ages. The consequences of health, sickness, accidents, disability, and death for the size, composition, and structure of the population are projected. Medical demography is also integrally concerned with the economic, social, and policy impacts of these dynamics.

Medical demography proceeds by examining the factors that explain variations in health and functional transitions across populations, taking into account the factors that influence health and longevity of the individual.

The link between the risk factors of individuals and the effects on population-level outcomes is a central focus of the discipline. Medical demography estimates the multiplicity of consequences attributable to diseases---singly and in interaction with one another---and the elimination or control of each. Medical demography describes and measures effects not only by changes in incidence and prevalence, but also by the contribution of changes in incidence and prevalence to the disease-alteration patterns of comorbid conditions and disability, as well as to future shifts in relative risk, population structure, social structures, and health care systems. The complexity of such estimations warrants the increasing reliance of medical demography on the construction and application of analytically rigorous models capable of combining several data sets derived from the same or similar populations.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications for research grants may be submitted by public and private, for-profit and non-profit organizations, such as universities, colleges, hospitals, and laboratories. Women and minority investigators, in particular, are encouraged to apply. Foreign institutions may apply, but are advised to consult National Institute on Aging (NIA) staff before applying and are strongly encouraged to apply in collaboration with a U.S. institution. Foreign institutions are only eligible for the research (R01) and conference grant (R13) mechanisms.

### MECHANISMS OF SUPPORT

The primary mechanisms for support of this initiative are the research project grant (R01), program project grant (P01), First Independent Research Support and Transition (FIRST) Award (R29), conference grant (R13), and Special Emphasis Research Career Award in Demography and Economics (K01).

### RESEARCH OBJECTIVES

Medical demography, which implicitly acknowledges the recursive relationship between disease structure and population structure, presents a unique context within which to examine the determinants and consequences of many chronic diseases of aging. It is especially useful for both scientific and public policy research into the complex impacts of the dementias and cognitive impairments of aging.

This announcement specifically focuses upon the dementias associated with aging (including AD) and related cognitive impairments without specific diagnoses. Investigators may also, however, propose research in which medical demographic methods are applied to other chronic diseases associated with aging.

Areas for general research efforts by medical demography include determination of how the incidence and prevalence of these disorders are influenced by specific demographic variables of the population, such as size, age composition, and socioeconomic characteristics. Building on the contributions of epidemiologic, clinical, and related research,



medical demographers should translate data on individual-level risk-factor modification into population-level projections for these disorders. Such analyses and projections are necessary for operationalizing new clinical and epidemiologic findings in estimates of the savings associated with postponing or elimination of AD and other dementias of aging, the effects of AD and cognitive impairment on prospective trends in active and disabled life expectancy, and on needs for long-term care at home and in institutional settings.

Examples of specific substantive research activities of interest include, but are not limited to:

- o Estimating the impact of dementias on healthy and institutionalized life expectancy;
- o Estimating the consequences of controlling mortality associated with other specific chronic diseases among the elderly for the distribution, severity, and duration of AD and other dementias in this population;
- o Employing methods of stochastic processes to improve current population estimates and future projections of AD and other dementias, especially as they relate to the estimation of demand for long-term care in institutional and home settings;
- o Clarifying the relationship between AD (and other dementias), associated comorbid conditions, and the decision to institutionalize;
- o Estimating the impact of demographic processes and changes on the future distribution of, and responses to, AD and other dementias with respect to:
  - available familial and household caregiving resources, especially of spouses and adult children
  - employment/caregiving trade-off patterns of adult children and consequences for foregone earnings and retirement income
  - duration of in-home care under various mixes of caregiver types and services
  - determinative effect of disease progression on rate and intensity of in-home care and on rate of institutionalization;
- o Estimating the nature, patterns, and rates of dissavings among persons with AD, and:
  - the impact on the household in which they reside
  - the differences from dissavings among the aged without AD
  - the effect of institutionalization on dissavings.
- o Clarifying the precise way in which any of the foregoing estimates of the medical-demographic distributions and other aspects of dementias are likely to have a differential impact in minority or rural populations or among the oldest old.

Investigators are encouraged to consider undertaking secondary analyses of existing data sets or those being developed, from epidemiologic surveys of AD supported by the NIA. When undertaking such secondary analyses, investigators are encouraged to consider appropriate consultation with neuroscientists in the interpretation of relevant clinical aspects of data.

This PA does not replace, but rather supplements, previous PAs of the NIA, including: Forecasting Life and Health Expectancy in Older Populations (NIH Guide for Grants and Contracts, Vol. 20, No. 34, September 13, 1991); Economics of Aging, Health, and Retirement (NIH Guide for Grants and Contracts, Vol. 20, No. 15, April 12, 1991) especially for economic costs of illness; Oldest Old (NIH Guide for Grants and Contracts, Vol. 13, No. 13, December 7, 1984); Epidemiology of Alzheimer's Disease and Other Dementing Disorders of Older Age (NIH Guide for Grants and Contracts, Vol. 15, No. 18, September 19, 1986); Demography and Economics of Aging (SERCA) (NIH Guide for Grants and Contracts, Vol. 20, No. 17, April 26, 1991); Alzheimer's Disease and Related Disorders: Issues in Caregiving (NIH Guide for Grants and Contracts, Vol. 18, No. 6, February 24, 1989).

Applicants are urged to obtain copies of these other relevant announcements from the Demography and Population Epidemiology Office (see INQUIRIES).

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study (see instructions for PHS 398 (rev. 9/91), page 22).

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority



groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale or studies on single minority population groups should be provided.

This policy applies to all studies submitted under this program announcement. The usual NIH policies concerning research on human subjects also apply. For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the applicant, the review will be deferred until the information is provided. Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application. All applications are required to address these policies. NIH funding components will not award grants that do not comply with these policies.

#### APPLICATION PROCEDURES

Applicants are to use the research project application form PHS 398 (rev. 9/91) that is available at the applicant's institutional research office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Westwood Building, Room 449, telephone (301) 496-7441. The title and announcement number, Medical Demography of Dementias of Aging, PA-92-88, must be typed in Section 2a on the face page of the application.

The application and five copies must be mailed or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Receipt dates are February 1, June 1, and October 1 of each year.

#### REVIEW PROCEDURES

R01 and R29 applications will be reviewed for scientific and technical merit by an appropriate Initial Review Group of the Division of Research Grants. All other applications (K01, P01, and R13) will be reviewed by an appropriate ICD review group. Secondary review will be by an appropriate National Advisory Council. Applications will compete on the basis of scientific merit and the traditional review criteria specific to each mechanism will apply.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that institute, center, or division. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Potential applicants are encouraged to discuss their project with NIA staff in advance of formal submission. This may be accomplished by calling or writing the program office listed below.

Direct inquiries regarding programmatic issues to:

Dr. Richard Suzman  
Demography and Population Epidemiology  
National Institute on Aging  
Gateway Building, Room 2C-234  
Bethesda, MD 20892  
Telephone: (301) 496-3136

For fiscal and administrative matters, contact:

Ms. Linda Whipp  
Grants and Contracts Management Office  
National Institute on Aging  
Gateway Building, Room 2N-212  
Bethesda, MD 20892  
Telephone: (301) 496-1472

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866. Agency Research Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241 and 41 USC 289) and be subject to PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

MAGNETIC RESONANCE SPECTROSCOPY AND CANCER TREATMENT

NIH GUIDE, Volume 21, No. 23, June 26, 1992

PA NUMBER: PA-92-86

P.T. 34; K.W. 0715035, 0706030

National Cancer Institute

The following corrections are made to this program announcement that was published in the NIH Guide for Grants and Contracts on June 12, 1992, Vol. 21, No. 22.

The NIH Guide reference in the heading contained the incorrect number and date; the correct information is NIH GUIDE, Vol. 21, No. 22, June 12 1992.

The first sentence of the third paragraph under Background Information, RESEARCH OBJECTIVES, should read as follows: "The goal of this initiative is to conduct well-focused, prospective clinical studies using currently available, routinely applicable, methodology to begin comprehensive testing of the potential for MRS to predict and/or detect therapeutic response in patients with tumors."

The first sentence of the second paragraph under Research Goals and Scope, RESEARCH OBJECTIVES, should read as follows: "This announcement seeks to encourage the following research topics in conventional MRI-guided MRS in preclinical and clinical cancer research."

The last paragraph under METHOD OF APPLYING is replaced with the following paragraph:

"If the application submitted in response to this RFA is substantially similar to a grant application already submitted to the NIH for review, but has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application cannot be submitted in response to this RFA that is essentially identical to one that has already been reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique."

## INQUIRIES

Questions and inquiries concerning this program announcement are to be directed to:

Faina Shtern, M.D.  
Chief, Diagnostic Imaging Research Branch  
Radiation Research Program  
National Cancer Institute  
Executive Plaza North, Suite 800  
Bethesda, MD 20892  
Telephone: (301) 496-9531

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816



# NIH GUIDE

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## For Grants and Contracts

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**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 24  
July 3, 1992

RICHARD W. HARRY

# 34-189  
\*\*5-35-1\*\*

201 WILL FOREST DRIVE  
BETHESDA MD 20892-1100

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES

TERMINATION AND PHASE OUT OF OUTSTANDING INVESTIGATOR GRANT AWARDS

NIH GUIDE, Volume 21, Number 24, July 3, 1992

P.T. 34; K.W. 1014006

National Cancer Institute

The National Cancer Institute (NCI), with the concurrence of the National Cancer Advisory Board, announces plans for the orderly phase out and termination of its Outstanding Investigator Grant (OIG) program. All non-competing commitments for future year support made to current grantees will continue to be honored as indicated on the current Notice of Award.

This announcement makes permanent the moratorium on new (Type 1) applications announced previously (NIH Guide Vol. 21, Number 14, April 10, 1992). Any Type 1 OIG awards made in Fiscal 1993, based on previously reviewed applications, will be for a 7-year project period and will be non-renewable as an OIG as a condition of award.

Currently funded OIG investigators who already have submitted either original or amended competing continuation applications (Type 2) for the June 1, 1992 receipt date for consideration at the January 1993 National Cancer Advisory Board meeting will be considered to have submitted a final competing application. Competitive but unfunded Type 2 applications from that Board round will be kept in an eligible status for an additional fiscal year. Therefore, such applicants will not be permitted to submit an amended competing continuation application for the subsequent receipt date. Where necessary to allow an orderly transition to other support, OIG grantees may request administrative extensions without additional funds for up to one year.



For all other current OIG awardees, a final round of Type 2 competing continuation applications will be accepted for the June 1, 1993 receipt date under the conditions specified below. This will be the last competing receipt date for the program prior to its termination.

1. Only investigators whose current OIG awards will be in the -05 or -06 year in Fiscal 1993, and who have not submitted a competing application for the June 1992 receipt date, may submit a final, non-renewable competing continuation application on June 1, 1993, requesting up to seven years of additional support starting on the next closest anniversary date of the current award. The first competing year proposed budget may not be increased more than 15 percent over the last non-competing (-07) year actual award. Applications requesting a budgetary increase of greater than 15 percent above the -07 year level will be accepted only with the prior approval of the NCI Executive Committee. Periods of time less than seven years may be requested for this class of application.

2. Any other investigator holding a non-competing Type 5 NCI OIG award may, regardless of current non-competing years remaining, at his/her own option, submit for the June 1, 1993 receipt date a final, non-renewable competing continuation application requesting five additional years of support, with the new budget period to commence from the next closest immediate anniversary date of the current grant period following selection for funding. This submission will not place at risk the current award, should the competing continuation application fail to be funded. The first competing year budget may not request more than a 10 percent increment over the comparable recommended budget level in the current award. Future year requests may not exceed current NIH award increment policies.

Although funds for these awards are provided for in the projected plans of the NCI, given the uncertainties of budgets for future fiscal years, it would be prudent for all applicants to submit individual research project grant applications (e.g., R01 or P01) at the appropriate time as alternative potential means of support should the competing continuation OIG application not be funded.

Current OIG awardees are strongly encouraged to contact the NCI program official identified on the Notice of Award to discuss future options for the transition from support under the OIG to support under other investigator-initiated grant mechanisms.

#### INQUIRIES

For additional information or for questions concerning this notice, contact:

Mrs. Barbara S. Bynum  
Director, Division of Extramural Activities  
National Cancer Institute  
Building 31, Room 10A03  
Bethesda, MD 20892  
Telephone: (301) 496-5147  
FAX: (301) 402-0062

#### COORDINATING CENTER FOR THE STUDY OF BETA-2 AGONIST THERAPY FOR ASTHMA

NIH GUIDE, Volume 21, Number 24, July 3, 1992

RFP AVAILABLE: NHLBI-HR-92-20

P.T. 34; K.W. 0715013, 0755018

National, Heart, Lung, and Blood Institute

Release of the solicitation previously published as Request for Proposals (RFP) NHLBI-HR-92-20, Coordinating Center for the Study of Beta-2 Agonist Therapy for Asthma, is hereby suspended for approximately three to four months. The National Heart, Lung, and Blood Institute will continue to accept requests for RFP NHLBI-HR-92-20 and will forward same as soon as it becomes available. A future announcement will be made in this publication identifying the release date of the RFP. Inquiries may be directed to:

Pamela S. Randall  
Contracts Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 654  
5333 Westbard Avenue  
Bethesda, MD 20892

## NOTICES OF AVAILABILITY (RFPs AND RFAs)

### THE ROLE OF THE FAMILY IN PREVENTING AND ADAPTING TO HIV INFECTION AND ACQUIRED IMMUNODEFICIENCY SYNDROME

NIH GUIDE, Volume 21, Number 24, July 3, 1992

RFA AVAILABLE: MH-92-11

P.T. 34; K.W. 0715008, 0730010, 0745027

National Institute of Mental Health  
National Institute on Drug Abuse  
National Institute on Alcohol Abuse and Alcoholism

Letter of Intent Receipt Date: August 15, 1992  
Application Receipt Date: September 15, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

#### PURPOSE

The purpose of this RFA is critical because little information is currently available about family processes on a wide variety of family configurations, including those that are at high risk for Human Immunodeficiency Virus (HIV) infection. In this RFA, the term "family" refers to the breadth of family configurations, including biological kin networks and non-related persons who consider themselves to be family through a "network of mutual commitment." Thus, family level of analysis may include the family of origin, family of choice, or a combination of these. Results from studies funded under this RFA will be used to develop effective prevention efforts aimed at high risk individuals and their families or to enhance treatment efforts for families already coping with HIV infection.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This effort is in accordance with the specific objectives 18.1 to 18.6, 18.8, 18.9, and 18.12. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202 783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by public and private, non-profit and for-profit organizations such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply.

#### MECHANISM OF SUPPORT

Support for applications submitted in response to this announcement will be through individual research projects (R01) of up to three years duration.

#### FUNDS AVAILABLE

In fiscal year 1993, a minimum of \$1.8 million has been set aside for this RFA. The NIMH will provide a minimum of \$1.4 million; the NIDA and the NIAAA will each contribute a minimum of \$.2 million to support three to five awards. Support may be requested for a period of up to three years. Continuation, noncompeting awards will be made, subject to availability of funds and progress achieved.

#### RESEARCH OBJECTIVES

The HIV epidemic not only takes a toll on the health of those directly infected but also affects the health and well-being of those close to them. Family members are likely to experience the stress of being caregivers or confidants while the AIDS patient is ill and experience grief upon the patient's death. Several examples from existing literature illustrate the potential radiating effects of AIDS on family members: parental death has been found to have adverse effects on surviving children's mental health; family members caring for older persons with dementia have been found to suffer depression and compromised immune functioning.

Methodology development may be necessary to capture meaningful data on non-traditional family relationships and structures in terms of membership, relationship roles, and patterns of interaction and communication. Study designs may need to clarify the nature of interactions between a family of origin, family of choice, and intimate support networks. Innovations in statistical analysis approaches may also be required to describe clearly these family processes.

The following sections suggest areas of research to meet the health promotion and disease prevention objectives outlined above. Researchers responding to this RFA, however, need not limit themselves to these topics.

**Ethnic and Cultural Considerations:** Cross-cultural variables deserve special consideration; the explicit investigation of cultural factors as an aspect of family adaptation to HIV infection is encouraged.

**Family Processes and the Course of Illness:** Basic information on family systems and processes for all subpopulations of persons infected with HIV is needed to determine what family factors serve to increase or decrease risk factors for becoming infected and to minimize symptomatology (physical and mental health outcomes) at all points in the course of the illness.

#### STUDY POPULATIONS

##### NIH/ADAMHA POLICY CONCERNING INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

Applications for grants and cooperative agreements and proposals for contracts that involve human subjects are required to include minorities and both genders in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages. If one gender and/or minorities are excluded or are inadequately represented in this research, particularly in proposed population-based studies, a clear compelling rationale for exclusion or inadequate representation should be provided. The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH and ADAMHA recognize that it may not be feasible or appropriate in all research projects to include minority populations (i.e., American Indians or Alaskan Natives, Asians or Pacific Islanders, Blacks, Hispanics). Investigators must provide the rationale for studies on single minority population groups.

Applications for support of research involving human subjects must employ a study design with minority and/or gender representation (by age distribution, risk factors, incidence/prevalence, etc.) appropriate to the scientific objectives of the research. It is not an automatic requirement for the study design to provide statistical power to answer the questions posed for men and women and racial/ethnic groups separately; however, whenever there are scientific reasons to anticipate differences between men and women, and racial/ethnic groups, with regard to the hypothesis under investigation, applicants should include an evaluation of these gender and minority group differences in the proposed study. If adequate inclusion of one gender and/or minorities is impossible or inappropriate with respect to the purpose of the research, because of the health of the subjects, or other reasons, or if in the only study population available, there is a disproportionate representation of one gender or minority/majority group, the rationale for the study population must be well explained and justified.

The NIH/ADAMHA funding components will not make awards of grants, cooperative agreements or contracts that do not comply with this policy. For research awards which are covered by this policy, awardees will report annually on enrollment of women and men, and on the race and ethnicity of subject.

#### LETTER OF INTENT

Prospective applicants are requested to submit, by August 15, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIMH staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Office of AIDS Programs  
National Institute of Mental Health  
5600 Fishers Lane, Room 15-95  
Rockville, MD 20857

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for this grant. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

#### Budget

Applicants must submit an adequately justified budget for each 12-month segment of requested support. Applicants are encouraged to include travel costs for three investigators from each site to attend one meeting each year (in Rockville, MD) in their budgets.

The signed original and five legible copies of the completed application must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

The single receipt date is September 15, 1992.

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by an initial review group (IRG) composed primarily of non-Federal scientific experts convened by the Alcohol, Drug Abuse, and Mental Health Administration. Final review is by an appropriate National Advisory Council; review by Council may be based on policy considerations as well as scientific merit. Only applications recommended by Council will be considered for funding. Summaries of the IRG outcomes are sent to applicants as soon as possible following IRG review.

#### AWARD CRITERIA

In the decision to fund applications, the following will be considered:

- o scientific merit as determined during the peer review process;
- o availability of funds;
- o balance among target populations with priority given to understudied populations;
- o balance among theoretical and multicultural approaches; and
- o balance among geographic areas.

#### INQUIRIES

Prospective applicants are strongly advised to contact an NIMH, NIDA, or NIAAA staff member in order to discuss the proposed research project prior to submission.

Willo Pequegnat, Ph.D.  
Office of AIDS Programs  
National Institute of Mental Health  
Parklawn Building, Room 17C-06  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-7281



Vincent Smeriglio, Ph.D.  
Clinical Medicine Branch  
Division of Clinical Research  
National Institute on Drug Abuse  
Parklawn Building, Room 11A-33  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-1801

Kendall Bryant, Ph.D.  
Program Director for AIDS Studies  
Prevention Research Branch  
National Institute on Alcohol Abuse and Alcoholism  
Parklawn Building, Room 13C-23  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-6177

For further information on grants management issues, applicants may contact:

Stephen J. Hudak  
Chief, Grants Management Section  
National Institute of Mental Health  
Parklawn Building, Room 7C-23  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-4456.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance 93.242, 93.273, and 93.279. Under statutory authorities of Sections 301 and 504 of the Public Health Service Act, (42 U.S.C. 241 and 290aa), the National Institute of Mental Health, the National Institute on Drug Abuse, and the National Institute on Alcohol Abuse and Alcoholism will accept applications in response to this request under the single receipt date of September 15, 1992. Grants are administered in accordance with the PHS Grants Policy Statement (revised October 1, 1990). Federal regulations at 42 CFR Part 52, "Grants for Research Projects," and Title 45 CFR Parts 74 and 92, generic requirements concerning the administration of grants, are applicable to this award.

#### DEVELOPMENT GRANT: ENVIRONMENTAL HEALTH SCIENCES CENTERS

NIH GUIDE, Volume 21, Number 24, July 3, 1992

RFA AVAILABLE: ES-92-02

P.T. 04; K.W. 0725005, 0710030, 0408006

National Institute of Environmental Health Sciences

Letter of Intent Receipt Date: August 14, 1992  
Application Receipt Date: September 4, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS A BRIEF SUMMARY OF ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS SHOULD OBTAIN THE RFA AND THE ENVIRONMENTAL HEALTH SCIENCES CENTER GRANT APPLICATION GUIDELINES FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The overall intent of this National Institute of Environmental Health Sciences (NIEHS) program is to establish multi-disciplinary research programs supported by a core center (P30). The focus is on environmentally related health problems of economically disadvantaged and/or underserved populations. The first step in this process is the current RFA that requests developmental grant (P20) applications from institutions or consortia of institutions wishing to develop multi-disciplinary core center (P30) grants with this theme.

This RFA has a single receipt date, September 4, 1992. However, the NIEHS intends to announce additional receipt dates for developmental grants on this theme periodically.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Developmental Grant: Environmental Health Sciences Centers, is related to the priority area of environmental health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private. Applications from minority individuals and women are encouraged.

### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) exploratory grant (P20). The maximum requested amount of each application may not exceed \$175,000 direct cost per year. The total project period may not exceed three years. It is estimated that approximately one to three awards will be made.

It is important to note that the award of a developmental grant by the NIEHS does not imply a commitment to future funding of any resulting research or center grant applications. These must be submitted separately and will be evaluated on the basis of their own merit. The core center (P30) grant requires a research grant base of at least \$1,000,000 of outside peer reviewed awards related to environmental health problems, particularly focusing on economically disadvantaged and/or underserved populations. Therefore, it will require a substantial effort during the award period of the P20 grant to achieve the level of research support base necessary to qualify and compete successfully for a core center grant.

### FUNDS AVAILABLE

The funding level for NIEHS developmental grants will be \$175,000 direct costs per year for a maximum of three years. It is anticipated that one to three developmental grants will be awarded depending upon the appropriation of funds for this purpose and the quality of the applications received. The awards are not renewable and supplements are not allowed.

### RESEARCH OBJECTIVES

Most Americans want to live long and healthy lives, and the majority achieve that goal. In general, however, economically disadvantaged and/or underserved populations are less likely to achieve this goal. At every stage of life, these populations suffer disproportionate levels of morbidity and mortality.

The primary purpose of the NIEHS developmental grants will be to provide support for a group of investigators to develop interdisciplinary collaborations and strategies, to obtain preliminary results to demonstrate feasibility, and to develop a research program addressing the above-cited PURPOSE of the NIEHS in this RFA. The resulting program will then be used as the basis for an application for other NIEHS project grants and ultimately a core center grant (P30). The objectives for an NIEHS developmental grant may include, but are not limited to:

- o Preliminary or feasibility studies to gather sufficient data to demonstrate the potential of an idea or the validity of an approach, to acquire or demonstrate technical competence, or to evaluate other technical factors involved in the development of a project that addresses the goal of this initiative;
- o Recruitment of new investigators whose expertise would strengthen the overall research project base in a subsequent core center grant application;
- o Inter- or intra-institutional planning to develop research strategies, including the establishment of a timetable or milestones, for the development of grant applications that are prerequisite for the NIEHS Core Center grant application.

### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by August 14, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIEHS staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

Christopher O. Schonwalder, Ph.D.  
Chief, Scientific Programs Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233, 104 Alexander Drive  
Research Triangle Park, NC 27709

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Applications must be received by September 4, 1992. The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on Line 2a of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the application, including the Checklist, and five signed, photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by DRG staff and responsiveness by NIEHS staff. Incomplete or non-responsive applications will be returned to the applicant without further consideration.

Site visits as part of the initial review of applications are not planned. Therefore, it is imperative that the application be complete and stand on its own merits. If a greater number of applications are received than anticipated, the NIEHS will utilize a triage process whereby the applications are given a preliminary scientific review by scientific peers in order to identify the most meritorious applications. Those applications identified as highly meritorious will be given a full scientific review and a complete and detailed summary statement will be prepared. Those applications not achieving these qualifications will not be given a full review and an abbreviated summary statement listing the reasons for this decision will be prepared.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Christopher O. Schonwalder, Ph.D.  
Chief, Scientific Programs Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7634

Direct inquiries regarding fiscal matters to:

Mr. David L. Mineo  
Grants Management Officer  
Grants Management Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-1373

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.894. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 43 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### DEVELOPMENT OF HIGH CONNECTIVITY NONMAMMALIAN MODELS

NIH GUIDE, Volume 21, Number 24, July 3, 1992

PA NUMBER: PA-92-89

P.T. 34; K.W. 0755020, 1002002, 1004005

National Center for Research Resources

#### PURPOSE

The Biological Models and Materials Research Program (BMMRP) of the National Center for Research Resources (NCRR) is reissuing this program announcement to encourage the submission of applications for the development of high connectivity nonmammalian models for biomedical research.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) Award.

#### MECHANISMS OF SUPPORT

The support mechanisms for this program will be the individual investigator-initiated research project grant (R01) and the FIRST Award (R29). Under these mechanisms the applicant will plan, direct, and carry out the research program. The proposed project period during which the research will be conducted should adequately reflect the time required to accomplish the stated goals and be consistent with the policy for grant support.

#### RESEARCH OBJECTIVES

The objective of this program announcement is to stimulate research on the development of high connectivity nonmammalian models for biomedical research as follows:

- o Organismic, including all poikilotherms, but not homeotherms, lower organisms (such as fishes, invertebrates, and microorganisms).
- o In vitro systems such as established cell lines from any species or cell or tissue culture from poikilothermic sources.
- o Mathematical or computer models, in particular if closely coupled to biological experimentation. There are opportunities for mathematical modeling in many areas of biomedical research and at all levels of biological organization.



A high connectivity model is one in which:

- o The body of knowledge about the system is large and has resulted in extensive cross information, or connection, with other systems. Examples of organisms that have many characterized properties or functions include, but are not limited to, *Drosophila melanogaster*, *Caenorhabditis elegans*, *Escherichia coli*, *Aplysia* sp., *Xenopus* sp., *Arabidopsis* sp., and sea urchins.
- o A function or property is broadly retained across many taxa. Examples include cytoskeletal structure, cell adhesion, cytochrome c, hormones, hormone receptors, and genetic regulation.
- o The research involves broad intertaxonomic projects.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit, i.e., June 1, October 1, and February 1.

Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

To identify the application as in response to this announcement, check "yes" in item 2a on the face page of the application and enter the PA number and the title, "High Connectivity Nonmammalian Models".

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be received by the National Institutes of Health (NIH), Division of Research Grants (DRG), and referred to an appropriate Initial Review Group (IRG) for scientific and technical review. Institute assignment decisions will be governed by customary programmatic considerations as specified in the NIH Referral Guidelines. Some applications may receive secondary assignments. Following the initial scientific review, the applications will be evaluated by the National Advisory Research Resources Council or another appropriate institute council/board.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that ICD. The following will be considered when making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Louise E. Ramm, Ph.D.  
Director, Biological Models and Materials Research Program  
National Center for Research Resources  
Westwood Building, Room 8A07  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 402-0630



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Direct inquiries regarding fiscal matters to:

Ms. Mary V. Niemiec  
Supervisory Grants Management Specialist  
Office of Grants and Contracts Management  
National Center for Research Resources  
Westwood Building, Room 849  
Bethesda, MD 20892  
Telephone: (301) 496-9840

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.198. Awards are made under authorization of the Public Health Service Act, Title III, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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## For Grants and Contracts

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Building 31, Bethesda, Maryland 20892

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21, No. 25  
July 10, 1992

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National Institutes of Health

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This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.

## NOTICES

### RESEARCH SUPPLEMENTS TO PROMOTE REENTRY INTO BIOMEDICAL AND BEHAVIORAL RESEARCH CAREERS

NIH GUIDE, Vol. 21, No. 25, July 10, 1992

P.T. 34, II; K.W. 0710030, 1014006

National Institutes of Health

Application Receipt Date: August 15, 1992

#### PURPOSE

The Office of Research on Women's Health and the Office of Extramural Research, National Institutes of Health (NIH), wish to announce the initiation of a pilot program to encourage fully trained women and men to reenter an active research career after taking time off to raise children or to attend to other pressing personal or family needs. This program will provide administrative supplements to existing NIH research grants for the purpose of supporting a full-time or part-time research experience tailored to refresh existing research skills and knowledge.

#### BACKGROUND

The NIH is concerned about the appropriate and adequate representation of women and minorities in biomedical and behavioral research careers. Adequate representation of diverse segments of the population is essential to ensure a thorough consideration of research issues of broadest interest to the populace of the United States. Over the years, the NIH has launched a number of special programs to encourage individuals from ethnic minority groups to enter research careers. No comparable programs have been developed to encourage women to enter research careers. This has been, in part, because the portion of NIH predoctoral and postdoctoral research training positions filled by women has increased steadily over the past decade. Currently, women occupy more than 40 percent of the predoctoral and postdoctoral research training positions supported by the NIH.

In spite of the increasing participation of women in research training, women constitute only 19 percent of the pool of NIH Principal Investigators. It is believed that the low representation of women may be in part related to the fact that women bear a preponderance of the responsibilities surrounding child rearing and family care. The NIH is, therefore, launching a new program specifically designed to offer opportunities to women and men who have interrupted their research careers to attend to family responsibilities such as child rearing. It is anticipated that the positions made available through this program will enable individuals to reestablish careers in biomedical and behavioral research.

#### GENERAL PROVISIONS

In all cases, the proposed research experience must be an integral part of the approved ongoing research of the parent grant or cooperative agreement. The individual supported under this supplemental award, hereafter called the candidate, must be given the opportunity to act as a full participant in the research project and must be given an opportunity to enhance and refresh her or his research capabilities to assist the development as an independent, competitive research investigator. Supplemental awards will be consistent with the goal of strengthening the existing research program and with the overall programmatic balance and priorities of the funding component of the NIH. Awards will be made according to the policies and provisions stated in this announcement.

Principal Investigators are encouraged to contact the appropriate NIH staff identified in the INQUIRIES section prior to submission in order to obtain specific information about application characteristics and submission requirements.

Administrative supplements provided under this program may be for either part-time or full-time support for the candidate provided all supported time is spent updating and enhancing research skills in preparation for an independent research career. Generally, part-time appointments may not be less than 20 hours per week.

Supplemental awards may not exceed \$50,000 in direct costs per year. A maximum of \$40,000 may be requested for salary and fringe benefits for the candidate. The amount of salary requested must be consistent with the policies of the grantee institution and must be related to the percent effort requested for the supplement. An additional amount up to \$10,000 may be requested for supplies and travel. Equipment may not be purchased except in unusual circumstances, and not without prior approval of the NIH awarding component.

The Office of Research on Women's Health estimates that \$1,000,000 will be available for 10 to 15 supplemental awards in FY 1992.

#### ELIGIBILITY REQUIREMENTS

**Grants and Cooperative Agreements:** The following active NIH awards at domestic institutions are eligible for Research Supplements to Promote Reentry into Biomedical and Behavioral Research Careers: R01, R10, R35, R37, P01, P50, P60, and U01. Principal Investigators on such awards are invited to submit a request for an administrative supplement to the awarding component of the parent grant to support an eligible candidate interested in reestablishing a research career. In all cases, the parent grant must have at least two years of support remaining at the time of a supplemental award. Usually, a parent grant would support only one administrative supplement including Research Supplements for Underrepresented Minorities, Research Supplements to Promote the Recruitment of Individuals with Disabilities into Biomedical Research Careers, and the Research Supplement to Promote Reentry into Biomedical and Behavioral Research Careers.

**Candidates:** Candidates for support under this program must have completed a doctoral degree, such as an M.D., D.D.S., Ph.D., or equivalent, and must have interrupted her or his training or career development to raise children or to attend to other family responsibilities. In most cases, candidates will have completed or nearly completed postdoctoral research training and will have had sufficient experience to be appointed at a staff or faculty level. Candidates must be able to demonstrate the potential to establish an independent research career by providing evidence of excellence prior to the career hiatus. It is expected that most of the applicants for this program will be women, since women are more likely to interrupt their careers to attend to family responsibilities, but men who satisfy these criteria also are eligible to apply.

This pilot program is not designed to provide an opportunity for additional postdoctoral research training. Individuals interested in further postdoctoral training are encouraged to consider National Research Service Award research training grants and fellowships or NIH research career awards. Information about such awards may be obtained from the Office of Grants Inquiries at telephone (301) 496-7441.

In most cases, the candidate will not have been an independent Principal Investigator on a traditional research grant (R01, R29), a project leader on a component of a program project or center grant (e.g., P01, P50), or a Principal Investigator on an individual Research Career Development Award (K04). The candidate, however, may have previously received NIH support for research training (e.g., T32, F32), early career development (K08, K11, K12, K15, K16), or may have received research support from Minority Biomedical Research Support (S06) or a small grant (R03).

Candidates must be citizens or non-citizen nationals of the United States or have been lawfully admitted for permanent residence (i.e., in possession of an Alien Registration Receipt Card) eligible for this award. It is recognized that individual circumstances vary, and for unusual situations, NIH program administrators should be consulted for a determination of eligibility.

#### APPLICATION PROCEDURES

A request for this supplement must be submitted by August 15, 1992. In making requests, the grantee institution, on behalf of the Principal Investigator of the parent grant and in cooperation with the candidate, must submit the request for supplemental funds directly to the awarding component that supports the parent grant. The request is not to be submitted to the NIH Division of Research Grants. Principal Investigators are encouraged to obtain the address for submission from the NIH program administrator of the parent grant.

The request for a supplemental award must include the following:

(1) a completed face page (with appropriate signatures) from Grant Application Form PHS 398 (Rev. 9/91). Include the title and grant number of the parent grant and the type of supplement being requested on line 1;

(2) a brief three to four page description, prepared by the Principal Investigator of the parent grant that includes:

(a) a summary or abstract of the funded grant or project,

(b) a description of the research experience proposed for the candidate,

(c) how the supplement will expand and foster the independent research capabilities of the candidate, and  
(d) how the proposed experience relates to the specific research goals and objectives of the parent grant;

(3) a signed statement from the candidate outlining her/his research objectives, career goals, and a description including the length of and the reason for the career hiatus;

(4) the social security number and biographical sketch of the candidate that includes a curriculum vitae, publications, and other evidence of scientific achievement;

(5) a signed statement from the Principal Investigator establishing the eligibility of the candidate for support under this program including information on citizenship, previous research experience, a description of how the candidate will contribute to the goals of the parent grant, and the plan to provide the necessary experience for the candidate to reenter a productive research career;

(6) a proposed budget entered on budget pages from the Grant Application Form PHS 398, related to the percent effort (where appropriate) for the research experience of the candidate during the first and future years. If the initial budget period requested is less than 12 months, the budget must be prorated accordingly;

(7) documentation, if applicable, that the proposed research experience is approved by the Institutional Animal Care and Use Committee (IACUC) or human subjects Institutional Review Board (IRB) of the grantee institution;

(8) if any of the research is to be conducted at a site other than the grantee institution, an appropriately signed letter from the institution where the research is to be conducted must also be submitted.

The request must be signed by the Principal Investigator, the candidate, and the appropriate institutional business official.

#### REVIEW CONSIDERATIONS

The staff of the particular awarding component will review requests for supplements using the following general criteria:

o the qualifications of the candidate including career goals, prior research training and experience, and potential to enter an independent research career;

o the plan for the proposed research experience in the supplemental request and its relationship to the parent grant;

o evidence from the Principal Investigator that the experience will enhance the research potential, knowledge, and/or skills of the candidate;

o evidence from the Principal Investigator that the activities of the candidate will be an integral part of the project.

#### FUNDING

The decision to fund a supplement will take six weeks from the time all the necessary information is received. In most cases during the first budget period, funds will be provided as an administrative supplement to the parent grant. In subsequent years, continued funding for the supplement is contingent on funding of the parent grant and cannot extend beyond the current competitive segment of the parent grant.

The continuation of support for the candidate in the remaining years of the competitive segment of the grant will depend upon satisfactory review by the NIH awarding component of progress for both the parent grant and the supplemental project, the research proposed for the next budget period, and the appropriateness of the proposed budget to the proposed effort.

For non-competing continuation applications, the progress report for the supplement must be clearly delineated from the progress report for the parent grant. The progress report in both non-competing and competing applications must include information about the research activities supported by the supplement even if support for future years is not requested.

#### INQUIRIES

Principal Investigators interested in participating in these programs are encouraged to contact NIH staff administering the parent grant. For general information about the research supplements, contact the following staff person of the appropriate awarding component:

#### NATIONAL INSTITUTE ON AGING

Deputy Associate Director  
Office of Extramural Affairs  
Building 31, Room 5C02  
Bethesda, MD 20892  
Telephone: (301) 496-9322



NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Assistant Director, Division of Extramural Activities  
Solar Building, Room 4C03  
Bethesda, MD 20892  
Telephone: (301) 402-0159

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

Director, Extramural Program  
Building 31, Room 4C32  
Bethesda, MD 20892  
Telephone: (301) 496-0802

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Special Assistant to the Deputy Director  
Building 31, Room 2A03  
Bethesda, MD 20892  
Telephone: (301) 496-0104

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

Director, Division of Extramural Activities  
6120 Executive Boulevard, EPS-400B  
Rockville, MD 20892  
Telephone: (301) 496-8693

NATIONAL INSTITUTE OF DENTAL RESEARCH

Director, Extramural Program  
Westwood Building, Room 503  
Bethesda, MD 20892  
Telephone: (301) 496-7723

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Assistant Director for Grants and Contracts  
Division of Extramural Activities  
Westwood Building, Room 657  
Bethesda, MD 20892  
Telephone: (301) 496-7793

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Director, Division of Extramural Research and Training  
Building 3, Room 301A  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7723

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Assistant Director, Referral and Liaison  
Westwood Building, Room 925  
Bethesda, MD 20892  
Telephone: (301) 402-0593

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Deputy Director, Division of Extramural Activities  
Federal Building, Room 1016  
Bethesda, MD 20892  
Telephone: (301) 496-4188

#### NATIONAL CANCER INSTITUTE

Director, Division of Extramural Activities  
Building 31, Room 10A03  
Bethesda, MD 20892  
Telephone: (301) 496-5147

#### NATIONAL EYE INSTITUTE

Research Training and Resources Officer  
Building 31, Room 6A49  
Bethesda, MD 20892  
Telephone: (301) 496-5983

#### NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Director, Division of Extramural Affairs  
Westwood Building, Room 7A17B  
Bethesda, MD 20892  
Telephone: (301) 496-7416

#### NATIONAL CENTER FOR NURSING RESEARCH

Director, Extramural Programs  
Building 31, Room 5B03  
Bethesda, MD 20892  
Telephone: (301) 496-0523

#### NATIONAL LIBRARY OF MEDICINE

Acting Associate Director, Division of Extramural Programs  
Building 38A, Room 5N505  
Bethesda, MD 20892  
Telephone: (301) 496-4621

#### NATIONAL CENTER FOR RESEARCH RESOURCES

Acting Deputy Director for Extramural Research Resources  
Building 12A, Room 4011  
Bethesda, MD 20892  
Telephone: (301) 496-6023

#### NATIONAL CENTER FOR HUMAN GENOME RESEARCH

Chief, Research Grants Branch  
Building 38A, Room 612  
Bethesda, MD 20892  
Telephone: (301) 496-7531

#### REVISED PHS 416-1 APPLICATION FORM AVAILABLE

NIH GUIDE, Vol. 21, No. 25, July 10, 1992

P.T. 22; K.W. 0720005, 1014006

National Institutes of Health

The newly revised Public Health Service Individual National Research Service Award application form -- PHS 416-1 -- is available. This revision, dated 10/91, and approved through 10/31/94, replaces the current version that was revised 7/88, reprinted with a 4/89 date, and approved through 4/30/91. Applicants should use the new form starting with the September 10, 1992, receipt date, although the older, 4/89 revision will be accepted for that deadline. Applicants submitting for deadlines after September 1992 must use the new form.

The newly revised fellowship application contains a number of changes that should facilitate the application process. Some of the more important changes include:

o The review and award schedule for the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) and the Agency for Health Care Policy and Research (AHCPR) has been added. ADAMHA and AHCPR use the same receipt dates as the National Institutes of Health (NIH), but have a different review and award schedule.

o The Introduction section has been expanded to provide information on the level of fellowships (predoctoral, postdoctoral, and senior) available at the three PHS funding agencies, and what, if any, budget information is requested in the application.

o Item 17. Applicant's Training/Employment, on form page 2, was modified to consolidate non-degree training, other research and professional experience, and employment into one item.

o A request for the name, institution, and department of individuals submitting reference letters was added to Section 3 of the Table of Contents, form page 3. This information will be helpful in avoiding potential conflict of interest situations in review.

o An explanation of the required documentation regarding gender and minority representation in study populations has been added to the instructions for the research proposal (page 10).

o The Assurances/Certifications sections on the Checklist page have been reformatted and updated. All the updates are in Section II-Sponsoring Institution, and include a revised Misconduct in Science assurance, and a new assurance on Age Discrimination.

To request two or more copies of the PHS 416-1 contact:

Administrative Services Office (PHS 416-1)  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 436  
Bethesda, MD 20892

To request a single copy of the PHS 416-1 contact:

Office of Grants inquiries (PHS 416-1)  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 449  
Bethesda, MD 20892

To assist delivery, please include a completed mailing label.

#### INQUIRIES

Questions regarding the use of the PHS 416-1 may be directed to:

Office of Grants Inquiries  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 449  
Telephone: (301) 496-7441

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### MASTER AGREEMENT FOR THE CLINICAL EVALUATION OF INVESTIGATIONAL ANTIEPILEPTIC DRUGS

NIH GUIDE, Vol. 21, No. 25, July 10, 1992

RFP AVAILABLE: NIH-NINDS-92-17

P.T. 34; K.W. 0740010, 0755015

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) intends to reissue a Master Agreement Announcement/Request for Proposals (MAA/RFP) entitled: "Master Agreement for the Clinical Evaluation of Investigational Antiepileptic Drugs," with the intent of seeking new sources to add to the current pool of

NIH Guide for Grants and Contracts - Vol. 21, No. 25, July 10, 1992

qualified Master Agreement (MA) holders. In May 1991, the NINDS issued MAA/RFP No. NIH-NINDS-91-10 to renew its MA Program for performance of future clinical evaluation studies of investigational antiepileptic drugs through January 1997. Approximately 39 Master Agreement awards were made as a result of that solicitation. In an effort to continually enlarge the pool of qualified holders under this program, the NINDS, each year, reissues the MAA/RFP. Current MA holders are not required to compete at this time. MAs will be awarded to those sources determined to be technically capable of performing clinical evaluations of investigational antiepileptic drugs in tolerability and preliminary efficacy studies, controlled efficacy and safety trials, or both, in patients with epilepsy. Only MA holders will be eligible to compete for future Master Agreements Orders that fund the actual clinical evaluation of specific drugs as they become available for testing.

This is not an MAA/RFP. MAA/RFP No. NIH-NINDS-92-17 will be issued on or about July 31, 1992, with a tentative closing date set for receipt of proposals on October 15, 1992.

The award of any MA under this RFP will be valid through January 31, 1997. The NINDS expects to add a number of new sources to its current pool of MA holders as a result of this MAA/RFP.

To receive a copy of MAA/RFP No. NIH-NINDS-92-17, submit a written request to the following address, and supply two self-addressed mailing labels:

Contracting Officer  
Contracts Management Branch, DEA  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 901  
7550 Wisconsin Avenue  
Bethesda, MD 20892

Attention: MAA/RFP No. NIH-NINDS-92-17

All responsible sources may submit a proposal that shall be considered by the Government.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### NLM FELLOWSHIP IN APPLIED INFORMATICS

NIH GUIDE, Volume 21, Number 25, July 10, 1992

PA NUMBER: PS-92-90

P.T. 22; K.W. 0720005, 1004017, 1004015

National Library of Medicine

##### PURPOSE

The National Library of Medicine (NLM) wishes to increase the national pool of health professionals capable of managing the knowledge and techniques of medical informatics in health science organizations. Medical informatics provides the theoretical and scientific basis for the application of computer and automated information systems to biomedicine.

Processing information faster and more efficiently, which today's technology can easily accomplish, is not sufficient. More intelligent processing, logical aggregation of information, synthesis, and analysis, and the development of knowledge systems that serve purposeful ends are needed.

The biomedical sciences and health-care professions can best make use of current information services and the emerging advanced automated systems by becoming involved in their development and use. Biomedical institutions urgently need a cadre of individuals properly educated in medical informatics at a level sufficiently scholarly to balance professional needs, technical judgments, and cost-benefit issues.

##### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, NLM Fellowship in Applied Informatics, is related to the priority area of educational and community based programs. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).



## ELIGIBILITY REQUIREMENTS

Applications on behalf of the fellows may be submitted by domestic non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Fellows must be citizens or non-citizen nationals of the United States, or have been lawfully admitted for permanent residence at the time of appointment. Individuals on temporary or student visas are not eligible. Individuals with a bachelor's, master's, or doctor's degree in a field related to health care, or enrolled in a program leading to such a degree, are eligible. It is not anticipated that this training will lead to a degree in most instances, although the training may be useful for credit or certification in certain other educational programs. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

The mechanism for support for fellowships under this program announcement is the individual fellowship (F37). The amount of the stipend to be paid shall be based on the salary or remuneration that the individual would have been paid on the date of award from the home institution, but in no case shall the award exceed \$50,000 per year, prorated on a monthly basis for awards shorter than 12 months. Stipends may be supplemented by an institution from non-Federal funds. Under no circumstances may the conditions of stipend supplementation detract from or prolong the training. In addition, the applicant's institution/organization may request an institutional allowance up to \$3,000 per year for support of supplies, equipment, travel, tuition, fees, insurance, and other training related costs. Training periods may be for one or two years.

## OBJECTIVES

Biomedical information is increasing at a rate so prodigious as to confound traditional techniques of information management. More and more, health-care professionals must rely on computers and telecommunications to help with storage, access, and appropriate use of the exploding mass of data that provides the basis of research and application in biomedicine. The theoretical and technical complexities of managing information with extraordinary new tools have fostered the field of applied medical informatics.

With support by the NLM, a number of universities now offer predoctoral and postdoctoral multi-disciplinary training in informatics with the goal of producing scientists capable of carrying out research in the myriad basic and applied problems of informatics. The NLM also offers individual fellowships in informatics research.

However, research alone is not enough. If informatics is to realize its full potential as an indispensable tool for researchers and health-care workers, there must be adequate numbers of health professionals able to apply the knowledge of informatics to: develop modern information systems in traditional organizations, use the new information techniques in a specific field, and help disseminate promising programs and systems. Accordingly, the NLM has developed a fellowship in applied informatics for health-care workers interested in learning and utilizing informatics in a relevant area of biomedicine.

Integrated Advanced Information Management Systems (IAIMS), networks and databases, effective use of high-speed communication links, electronic patient records, expert systems and decision-making aids for research and for clinical practice, computer-assisted instruction, clinical care outcome analysis, and a host of technological systems for medical libraries are but a partial list of applications that could be considered by a potential fellow.

## APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 416-1 (rev. 10/91) and will be accepted at the standard application deadlines as indicated in the application kit, January 10, May 10, and September 10.

Application kits are available at most institutional offices of sponsored research offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

Complete item 3 on the face page of the application indicating that the application is in response to this announcement and print APPLIED INFORMATICS.

The completed original and two legible copies along with the checklist, the Personal Data form, appendix material, sealed reference reports, and other required information must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892



## REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by the Biomedical Library Review Committee, in accordance with the standard NIH peer review procedures. The review criteria customarily employed by the NIH for fellowship applications will prevail. Following scientific-technical review, the applications will receive a second-level review by the NLM.

## AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to THE NLM. The following will be considered when making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Roger W. Dahlen, Ph.D.  
Biomedical Information Support Branch  
National Library of Medicine  
Building 38A, Room 5S522  
Bethesda, MD 20894  
Telephone: (301) 496-4221

Direct inquiries regarding fiscal matters to:

Brian Campbell  
Grants Management Officer  
National Library of Medicine  
Building 38A, Room 5N511  
Bethesda, MD 20894  
Telephone: (301) 496-4253

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, Medical Library Assistance, 93.879. Grants will be awarded under the authority of the Public Health Service Act, Section 472 (42 USC 286b-3) and administered under PHS grants policies and Federal Regulations, most specifically at 42 CFR Part 61 and 45 CFR Part 74.

This authority is separate and distinct from the National Research Service Award. Therefore, Section 487 of the Public Health Service Act, as amended (42 USC 288) and implementing regulations (42 CFR Part 66), requiring satisfactory assurance of meeting the service requirement is not applicable. While signature is still required on page 1 of the application, parts I, II, and III of the National Research Service Award Service Assurance are not included.

This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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5333 Westbard Avenue  
Bethesda, MD 20816

# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 26

July 17, 1992

RICHARD W MURRY

# 340189  
\*\*81350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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NOTICES OF AVAILABILITY (RFPs AND RFAs)

STUDIES ON ONCOGENE ACTIVATION AND MOLECULAR DOSIMETRY IN ANIMAL MODELS FOR CHEMICAL CARCINOGENESIS

NIH GUIDE, Volume 21, Number 26, July 17, 1992

RFP AVAILABLE: NIH-ES-92-30

P.T. 34; K.W. 0715035, 0785140

National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH), is soliciting proposals from offerors having the expertise to conduct studies concerning Oncogene Activation and Molecular



Dosimetry in Animal Models for Chemical Carcinogenesis. The Government estimates the project will last approximately 5 years and will require approximately 1,020 professional (Ph.D.) person-hours, 10,200 laboratory technician person-hours, and 20,400 animal technician person-hours.

The Request for Proposals (RFP) will be released on or about July 15, 1992, and proposals due to be received September 18, 1992. All responsible sources may submit a proposal that shall be considered by the agency.

Requests must reference RFP NIH-ES-92-30 and should be forwarded to:

National Institute of Environmental Health Sciences  
Contracts and Procurement Management Branch, OM  
ATTN: Mr. James Doyle, Contract Specialist  
79 T.W. Alexander Drive, 4401 Research Commons Building  
P.O. Box 12874  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7893  
FAX: (919) 541-2712

**PRENATAL DIAGNOSIS USING FETAL CELLS FROM MATERNAL BLOOD: CLINICAL TRIAL**

NIH GUIDE, Volume 21, Number 26, July 17, 1992

RFP AVAILABLE: NICHD-CRMC-92-15

P.T. 34; K.W. 0745020, 0775020, 0775025

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) is planning to conduct a clinical trial to continue the development and refinement of procedures for a non-invasive method of prenatal diagnosis of genetic disorders from maternal blood. Based on preliminary research and observations of a limited number of subjects, it is apparent that fetal aneuploidies may be identified from maternal peripheral blood by use of flow-sorted nucleated fetal erythrocytes and in-situ hybridization with chromosome specific probes. It is the intent of the NICHD to award a maximum of three contracts for the recruitment of approximately 3000 pregnant women to test the accuracy of the investigative prenatal diagnostic techniques. This will be accomplished by comparison of data obtained prenatally and postnatally and from information obtained through other prenatal diagnostic procedures such as amniocentesis and chorionic villus sampling (CVS). Only women already committed to amniocentesis or CVS will be considered for recruitment into this clinical trial.

The successful contractors will develop a common research protocol, further develop and refine investigative prenatal diagnostic techniques, recruit patients, compare data from the different prenatal diagnostic procedures, conduct data analysis, and publish the data acquired. The contracts are expected to be awarded for three and one-half years. This is a new solicitation for the further development and a clinical trial of the referenced methodologies. The issuance of the Request for Proposals (RFP) will be on or about August 11, 1992, and proposals will be due by 4:00 PM (local time) on October 13, 1992. Those organizations desiring a copy of the above RFP may send a written request to:

Ms. Virginia A. DeSeau  
National Institute of Child Health and Human Development  
6100 Building, Room 7A07  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-4611

All requests must cite the RFP number listed above and include two self-addressed mailing labels. All sources who consider themselves qualified may respond to this request.

**OZONE: MECHANISMS OF ACTION**

NIH GUIDE, Volume 21, Number 26, July 17, 1992

RFA AVAILABLE: ES-92-04

P.T. 34; K.W. 1007005, 1007009

National Institute of Environmental Health Sciences  
National Heart, Lung, and Blood Institute

Application Receipt Date: November 24, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

**PURPOSE**

The mission of the National Institutes of Environmental Health Sciences (NIEHS) is to provide scientific knowledge for the prevention and amelioration of untoward health effects due to exposure to environmental agents. Under the Clean Air Act (CAA) Amendments of 1990, the NIEHS has been directed to conduct a program of basic research related to the health effects of exposure to air pollution, particularly ozone, and to ensure that such programs do not conflict with research undertaken by the Administrator of the Environmental Protection Agency (EPA). In addition, the National Heart, Lung, and Blood Institute (NHLBI) has an interest in understanding the pathologic/biologic

changes resulting from inhalation of ozone. To this end, the NIEHS, NHLBI, and EPA participated in workshops convened for the specific purpose of identifying and assigning priorities to key research needs with an emphasis on the health effects and risks of chronic ozone exposure and the mechanisms by which exposure to elevated ozone levels exacerbates or amplifies lung diseases. In this context, chronic ozone exposure is considered to be a condition or a set of conditions that results from continuous exposure to ozone at or above current National Ambient Air Quality Standards levels for a relatively long period of time, the intermittent exposure at these levels of ozone repeatedly for a relatively long period of time, or some appropriate combination of the continuous and intermittent exposure over a long period of time.

The recommendations from the workshop were that aggressive research programs should be encouraged and supported in the following areas: (a) biomarkers of exposure and effect, (b) mechanisms of action, and (c) epidemiology. To address the problems identified, the NIEHS and the NHLBI solicit applications for studies related to the mechanisms of the health effects and better understanding of the risks associated with prolonged ozone exposure as well as the development of biomarkers that can predict the health effects.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Ozone: Mechanisms of Action, is related to the priority area of environmental health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

#### FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for the entire program is \$1.8 million. The expected number of awards is approximately nine; approximately six to be funded by the NIEHS and three by the NHLBI.

This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIEHS and the NHLBI, awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Support will not be provided under this RFA for research activities focussed exclusively on clinical trials or the initiation of large-scope epidemiologic studies.

#### RESEARCH OBJECTIVES

Ozone is the major oxidant in photochemical smog. The current ambient air quality standard in the USA for ozone is 0.12 ppm as a daily maximum with a one-hour averaging time, not to be exceeded more than four times in three years. This standard was based on the integration of scientific data available from controlled animal exposure studies, human exposure studies, and epidemiological studies that reported respiratory function impairment following short-term ozone exposure. However, recent EPA chamber studies have reported progressive decrement of lung function demonstrating that the effects of ozone on lung function, may be cumulative. For the most part, research has been conducted on healthy young subjects. The lung function effects appear to be dose-dependent where dose is a product of concentration, duration of exposure, and lung ventilation. The range of responses in both healthy and asthmatic subjects has been wide, the reproducibility of responses is not fully characterized, and the mechanisms underlying the dysfunctions are still unclear. It is not known whether ozone triggers the bronchoconstrictive response directly by altering the irritability of the airway smooth muscle or indirectly by the stimulation of receptors in the deep lung.

In summary, the combination of ozone concentration profiles, duration of exposure, lung ventilation, and frequency of ozone exposure that might bring about a change in human lung function is not well understood. The mechanisms responsible for the health effects are not clear. The human population is often exposed to ozone levels exceeding the standard for 6-11 hours repeatedly over a period of 1-4 days. These issues are important to public health and welfare, particularly to children, the aging population, and individuals with pre-existing respiratory disease conditions.

The goal of the NIEHS and the NHLBI in this solicitation is to determine the relationships and mechanisms of health effects of long-term environmental exposures to ozone. Basic research applications utilizing animal, clinical, and existing data from both epidemiological studies and large-scale health and air monitoring records are solicited. This research may include studies to identify the physiological effects of ozone exposure and studies to determine the underlying cause for such effects. Research toward understanding the chronic and relative permanency of health effects resulting from long-term and multiple exposure to ozone, the degree to which biological function has been compromised as a consequence of exposure, and the extent to which the health effects are physiologically and/or pathologically progressive or regressive is specifically requested. In the evaluation of these effects, it is

suggested that realistic levels of exposure to ozone be utilized. Although higher than normal ozone levels may be appropriate for parts of a study, the relevance of study objectives to human health will be used as review criterion for funding. In addition, encouragement is given to studies examining the time-course and persistence of the effects as well as individual sensitivity and responsiveness, e.g., seasonal and age variations, as well as pre-existing disease conditions. The use of existing information derived from epidemiological, human clinical and field studies, and animal models is also appropriate.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

Applications must be received at the NIH by November 24, 1992.

For developing programs that deal with clinical populations, applicants may wish to consider utilization of General Clinical Research Center (GCRC) facilities. More information on the GCRC program is available from Dr. Judith Vaitukaitis at the National Center for Research Resources, telephone: (301) 496-6595.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIEHS or NHLBI staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle. Review criteria for this RFA are generally the same as those for unsolicited research grant applications.

Primary and secondary assignments of applications submitted in response to this RFA will be made using the customary referral guidelines.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Direct inquiries and requests for the RFA to:

George S. Malindzak, Jr., Ph.D.  
Program Administrator, Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-3289/1379

or

James P. Kiley, Ph.D.  
Chief, Airways Diseases Branch  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 6A15  
Bethesda, MD 20892  
Telephone: (301) 496-7332

Mr. David L. Mineo  
Grants Management Officer  
Grants Management Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
104 T.W. Alexander Drive, P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-1373

and

Ms. Tanya McCoy  
Grants Management Officer  
Grants Management Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A17  
Bethesda, MD 20892  
Telephone: (301) 496-4970



## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.113 and 93.115. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 43 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## OLFACTORY EVOKED POTENTIALS

NIH GUIDE, Volume 21, Number 26, July 17, 1992

RFA AVAILABLE: DC-93-01

P.T. 34; K.W. 0705070, 1002030

National Institute on Deafness and Other Communication Disorders

Letter of Intent Receipt Date: October 26, 1992

Application Receipt Date: November 30, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMES IN INQUIRIES, BELOW.

## PURPOSE

The National Institute on Deafness and Other Communication Disorders (NIDCD) invites research grant (R01) applications focused on the application of olfactory evoked potentials to address basic and clinical research issues in the area of olfaction. The scope of studies applicable to the present RFA includes the identification of the cortical generators of the potentials, differentiation and control of olfactory and chemosensory trigeminal stimulation, and anatomic diagnosis of chemosensory disorders.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Olfactory Evoked Potentials, is related to several priority areas, including nutrition, environmental health, maternal and infant health, and cancer, as they relate to dysfunctions of the sense of smell. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

## FUNDS AVAILABLE

It is expected that \$725,000 will be available for the first year of support (direct and indirect costs) for the entire program and that from two to four applications will be funded. The level of support is dependent on the scientific merit and scope of the applications and the availability of funds.

## RESEARCH OBJECTIVES

### Background

Intensive research on visual, auditory, and somatosensory evoked potentials has provided a large body of valuable information on how various parts of the nervous system respond to a presented stimulus. For example, auditory evoked potentials have proved useful for differentiating sensory and neural hearing loss, for detecting tumors and other disease states affecting central auditory pathways, and for noninvasively detecting hearing loss in newborns and infants. In addition, development of new stimulus delivery systems and recording electrodes now permits the use of auditory brainstem responses for intraoperative monitoring of patients with head injuries.

In comparison to visual, auditory, and somatosensory evoked potentials, olfactory evoked potentials have received much less attention, and their development and application has progressed much more slowly. Investigators have often experienced considerable difficulties in controlling olfactory stimulation and have found it necessary to employ special olfactometers and procedures to present identical stimuli with steep rise and fall times, that is, stimulus delivery that produces approximate square waves. Precise delivery of the chemical stimulus must be achieved without altering the mechanical or thermal conditions at the stimulated mucosa. Some unwanted non-chemosensory events, notably neuromuscular events, can be eliminated by the use of a procedure in which the



stimulus is delivered intranasally and closure of the soft palate isolates the nasal cavity from the oral cavity. Cognitive events related to voluntary sniffing are also eliminated by this procedure.

To date, only late near-field olfactory evoked potentials have been recorded in humans. Although the site of the cortical generators of olfactory evoked potentials has not been identified, studies suggest that the generators originate from a neocortical olfactory projection area in the orbitofrontal cortex. Evoked magnetic field recordings indicate that responses to chemosensory trigeminal stimuli are generated in the secondary somatosensory cortex.

The topographical distribution of chemosensory evoked potentials appears to be useful in differentiating chemosensory trigeminal from olfactory activity. For example, after stimulation with ammonia, maximum amplitudes were recorded contralateral to the stimulated nostril; after stimulation with vanillin, little difference in amplitudes was seen between hemispheres. Measurements of latency and waveform complexity may also provide useful topographical information. Additional investigations of the topographical distribution of chemosensory evoked potentials could prove helpful in the interpretation of the psychophysical interactions between the trigeminal and olfactory systems and in the differentiation of olfactory and chemosensory trigeminal disorders.

At present, psychophysical techniques do not provide an anatomic diagnosis of chemosensory disorders. Hope for progress in this area of differential anatomic diagnosis has led to renewed interest in the clinical application of olfactory evoked potentials. Additional research is needed to determine the degree to which olfactory evoked potentials will attain fundamental research importance and clinical usefulness comparable to visual, auditory, and somatosensory evoked potentials.

#### Scope

This RFA is aimed at stimulating investigators to utilize olfactory evoked potentials to advance fundamental research and clinical research progress in the area of olfaction. Applicants must address specific hypotheses or research questions related to olfaction.

A wide spectrum of research topics is acceptable for this RFA. Studies may include those below. Investigators are encouraged to consider other topics relevant to this program.

- o Identify the cortical generators of olfactory evoked potentials and other chemosensory evoked potentials.
- o Differentiate olfactory disorders from chemosensory trigeminal disorders.
- o Identify the sites of anatomic damage in patients with olfactory disorders.
- o Investigate individual differences in the rate of adaptation as measured by olfactory evoked potentials.
- o Investigate the usefulness of olfactory evoked potentials for the diagnosis of dysosmia, hyperosmia, hyposmia, and anosmia.
- o Determine the effects of different odor qualities on olfactory evoked potentials.
- o Identify chemicals that differentially stimulate the various chemoreceptive systems in the nose.
- o Develop a measure of the olfactory epithelial potential analogous to the electroretinogram.

Close interactions are encouraged among investigators in and outside the field of olfaction and among those in various disciplines, including neurophysiology, psychophysics, otolaryngology, and other medical disciplines.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by October 26, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDCD staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Earleen Elkins  
Chief, Scientific Review Branch  
National Institute on Deafness and Other Communication Disorders  
Room 400-B, Executive Plaza South  
6120 Executive Boulevard  
Rockville, MD 20892

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441; and from the NIH program administrator named below under INQUIRIES.

Applications must be received by November 30, 1992. If an application is received after that date, it will be returned to the applicant.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources (NCRR) may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator may be included with the application.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIDCD staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NIDCD. The second level of review will be provided by the National Advisory Deafness and Communication Disorders Council.

#### AWARD CRITERIA

The anticipated date of award is July 1993.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Jack Pearl, Ph.D.  
Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-3464  
FAX: (301) 402-6251

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Division of Extramural Activities  
Grants Management Branch  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-0909  
FAX: (301) 402-6251

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ASTHMA AND ALLERGIC AND IMMUNOLOGIC DISEASES COOPERATIVE RESEARCH CENTERS

NIH GUIDE, Volume 21, Number 26, July 17, 1992

RFA AVAILABLE: AI-92-07

P.T. 04; K.W. 0715013, 0710070, 0710030

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: August 28, 1992  
Application Receipt Date: November 10, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN "INQUIRIES" BELOW.

#### PURPOSE

The Division of Allergy, Immunology and Transplantation (DAIT), National Institute of Allergy and Infectious Diseases (NIAID), invites applications for cooperative agreements to establish the Asthma and Allergic and Immunologic Diseases Cooperative Research Centers (AAIDCRC) program. This program is designed to support basic and clinical research on mechanisms of, intervention in, and prevention of asthma and allergic and immunologic

diseases. The applications are to be designed around a central scientific theme demonstrating relevance to one or more diseases in these areas. A minimum of three biomedical research projects must be proposed, plus a Demonstration and Education research component, to study asthma and allergic or immunologic diseases in defined populations. The NIAID plans to continue its support of the AAIDCRC program. Reissuance of this initiative in future years is anticipated, but not certain.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Asthma and Allergic and Immunologic Diseases Cooperative Research Centers, is related to the priority areas of education and community-based programs, environmental health, diabetes and chronic disabling conditions, and immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Foreign organizations are not eligible to apply. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

Awards will be made as cooperative agreements (U01s), a funding mechanism in which substantial NIAID programmatic involvement with the recipients during performance of the planned activity is anticipated. Applicants will be responsible for the planning, direction, and execution of the proposed projects. The total project period for applications submitted in response to the present RFA may not exceed five years.

## FUNDS AVAILABLE

The estimated total funds available for the first year of this program will be \$6,000,000. Budget requests should be limited to total direct costs of no more than \$500,000 per annum. In Fiscal Year 1993, the NIAID plans to fund approximately eight AAIDCRCs. The anticipated date of award is July 1993.

This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIAID, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

The purpose of the AAIDCRC program is to accelerate the development and application of fundamental knowledge of the immune system through support of investigations concerned with immune system mediated disorders, i.e., allergic, immunologic, and related inflammatory disorders. Specific goals of the Program are: (1) advancing the understanding of the etiology and pathogenetic mechanisms of allergic and immunologic diseases and (2) applying an expanded knowledge base to the development of improved measures of diagnosis, treatment, and prevention of a wide variety of allergic and immune system disorders.

Eligible topics for study relevant to asthma and allergic and immunologic diseases may include, but are not limited to: the basic pathophysiologic mechanisms of human allergy such as the role of cytokines and/or adhesion molecules in allergic inflammation and IgE responses; the identification, isolation, and characterization of etiologic agents of allergic and hypersensitivity reactions (e.g., airborne allergens, drugs, industrial chemicals, foods, and contact sensitizing agents); the pathophysiology, epidemiology, and genetics of allergic diseases (including allergic rhinitis, asthma, and atopic dermatitis); the pathophysiology of other hypersensitivity reactions (including allergic bronchopulmonary aspergillosis, hypersensitivity pneumonitis, food allergy, and drug reactions); immunodermatologic studies (many hypersensitivity and immune-mediated inflammatory mechanisms are relevant to disorders of the skin such as contact dermatitis, atopic dermatitis, and urticaria); genetic, cellular, and molecular mechanisms of immune system disorders including autoimmune diseases and immunodeficiency diseases; application of immunotherapeutics to immune system disorders; characterization of mechanisms of acute and chronic inflammation; immunopathologic aspects of host defense and phagocytosis; and normal and abnormal leukocyte and complement system functions.

Note: Studies of the human immunodeficiency virus (HIV), AIDS, and associated opportunistic infections and malignancies are not encompassed under this RFA.

Each AAIDCRC applicant is required to propose a demonstration and education (D&E) research component. Demonstration and education research involves testing the effectiveness of interventions to promote health or prevent disease in defined populations. Applicants may choose to: (1) Option 1: Propose an independent D&E research project on a topic of their own choosing for a total annual direct cost not to exceed \$75,000, or (2) Option 2: Propose participation as intervention test sites in NIAID-supported D&E research projects for a total annual direct cost not to exceed \$75,000.

## SPECIAL REQUIREMENTS

All applicants responding to this RFA must satisfactorily address the following:

1. The scientific merit and significance of each individual research project and the extent to which the proposed multiproject program will contribute to accomplishing the central scientific theme more efficiently and effectively than a series of independent, individually supported studies.



2. Evidence that the proposed AAIDCRC director is a senior scientist in the field(s) of asthma, allergic and/or immunologic diseases with the necessary experience to assume both leadership of the investigative group and responsibility for scientific and administrative functions. Evidence that each proposed project has a designated project leader with a demonstrated record of scientific accomplishment in the basic science disciplines or clinical specialties relevant to the proposed project.

3. Documentation of the sponsoring institution's commitment to the program, including support of membership of the proposed principal investigator on the AAIDCRC Executive Committee and willingness to abide by the selections made by the AAIDCRC Executive Committee on specific cooperative clinical and/or D&E research projects.

4. A description of available laboratory and clinical facilities, including specific information on the institution's present patient load and access to and projections for patient involvement in clinical investigations.

5. A description of ongoing relevant research studies, identifying existing projects and sources of support, and past research by members of the proposed investigative group relevant to the application.

6. Description of institutional expertise in, and collaboration/cooperation among, basic research and clinical specialties required to carry out the proposed projects.

7. A clear, concise plan that describes the interrelationships among the members of the AAIDCRC and the contribution of each to fulfillment of AAIDCRC objectives and includes an organizational chart showing the name, organization, and scientific discipline of the key personnel.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit by August 28, 1992, a letter of intent that includes a descriptive title of the overall proposed research, the name of the Principal Investigator, a list of the names of key investigators and their institution(s), and a descriptive title of each proposed research project. The letter of intent is requested to provide an indication of the number and scope of applications to be reviewed. The letter of intent is not binding and does not commit the sender to submit an application, nor is it a requirement for submission of an application. The letter of intent is to be sent to:

Mark L. Rohrbaugh, Ph.D.  
Scientific Review Administrator  
Microbiology and Immunology Review Section  
Scientific Review Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C22  
Bethesda, MD 20892  
Telephone: (301) 496-8424

#### APPLICATION PROCEDURES

Applications are to be submitted on the research grant application form PHS 398 (rev. 9/91). These forms may be obtained from most institutional sponsored research offices. If not available there, they may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone (301) 496-7441.

Applications must be received by November 10, 1992.

#### REVIEW CONSIDERATIONS

General review considerations are outlined in the NIAID Information Brochure on Program Projects, Centers, and Cooperative Agreements, which contains special instructions and information for preparing multiproject applications for cooperative agreements, including Review Procedures and Review Criteria, and other important information. This Brochure and the RFA are available upon request to the contact listed under INQUIRIES. Additional review criteria are outlined in the RFA.

Applications will be reviewed by NIAID staff to determine administrative and programmatic responsiveness to this RFA; those judged to be non-responsive or incomplete will be returned to the applicant without review.

Those applications that are complete and responsive may be subjected to a triage by an NIAID peer review group before or during the scientific review meeting to determine the scientific merit relative to other applications received in response to this RFA. The NIAID will withdraw from competition those applications judged to be non-competitive for award and will notify the applicants and institutional business officials.

Those applications judged by the reviewers to be competitive for award will be further reviewed for scientific and technical merit by a review committee convened by the Division of Extramural Activities, NIAID, in March 1993. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council in June 1993.



#### AWARD CRITERIA

The anticipated date of award is July 1993.

Funding decisions will be made on the basis of scientific and technical merit as determined by peer review, program needs and balance, and the availability of funds.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Dr. Marshall Plaut  
Chief, Asthma and Allergy Branch  
Division of Allergy, Immunology and Transplantation  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 4A23  
Bethesda, MD 20892  
Telephone: (301) 496-8973  
FAX: (301) 402-2571

Direct inquiries regarding fiscal matters to:

Mr. Jeffrey Carow  
Chief, Immunology Grants Management Section  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 4B29  
National Institutes of Health  
Bethesda, MD 20892  
Telephone: (301) 496-7075

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.855 - Immunology, Allergic and Immunologic Diseases Research. Grants are awarded under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### MAPPING THE MOUSE GENOME WITH EMPHASIS ON TECHNOLOGY DEVELOPMENT

NIH GUIDE, Volume 21, Number 26, July 17, 1992

RFA AVAILABLE: HG-92-002

P.T. 34; K.W. 0755045, 1002058

National Center for Human Genome Research

Letter of Intent Receipt Date: October 16, 1992

Application Receipt Date: November 13, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Center for Human Genome Research (NCHGR) invites applications for assistance awards to support research projects designed to increase the rate, resolution, and usefulness of genetic and physical maps of the mouse genome. The specific areas of interest are: (1) incorporation of significant numbers of genes identified by sequence-tagged sites (STSs) [Olson et al., Science 245: 1434, 1989] into the genetic map; (2) development of technology to facilitate the construction of physical maps; and (3) facilitation of the progress of other genetic and molecular biology projects that are map-based, by making mapping resources available to the community.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by for-profit and non-profit organizations, both domestic and foreign, public and private universities, medical colleges, research institutions, hospitals, and laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from women and minority scientists are particularly encouraged.

#### MECHANISM OF SUPPORT

Support for this program will be through individual research grants (R01s), pilot projects/feasibility studies (R21), and program project grants (P01s). Applicants may request support for up to five years. It is anticipated that 10 awards will be made representing a mix of research topics and grant mechanisms. This number may be increased if a large number of highly meritorious applications are received and if funds are available. The number

of awards made will be contingent upon the quality of applications received and the availability of funds.

#### FUNDS AVAILABLE

The total amount of support available for grants under this RFA will be \$3.0 million for the first year of the project and is contingent upon appropriation of funds for this purpose.

#### RESEARCH OBJECTIVES

All applications responsive to this RFA for genetic and physical mapping of the mouse genome and development of mapping resources to facilitate additional genomic and biological research must have as a primary goal: (1) the development of new or significantly improved technology; (2) strategies for increasing throughput for identifying and mapping markers; and/or (3) approaches that are rapid, efficient, and cost-effective. Below are examples of projects that would be considered responsive to this RFA.

##### A. Enhancement of the Mouse Genetic Map

Any project submitted in response to this section of the RFA must complement ongoing mapping activities and, where appropriate, make maximal use of existing resources, e.g., existing crosses and mapping reagents. Specifically, applications are encouraged in the following areas:

- o Improvement or development of sequence-based technologies to map genes and other functional elements rapidly, cost-effectively, and with a high rate of throughput.
- o Expansion of the genetic map to include genes identified by sequence-tagged sites (STSs); special attention should be given to identifying genes/markers for telomeres and areas where large gaps exist.

##### B. Technologies to Facilitate Development of the Physical Map

In the past several years, there have been many improvements in the development of strategies for constructing physical maps of mammalian genomes. However, many technical problems remain, such as the high level of chimerae in large-insert libraries of cloned DNA, rapid and accurate assembly of clones into contigs, closure of gaps between contigs, the existence of DNA fragments that are unclonable, and the cloning and ordering of highly repetitive DNA fragments. Therefore, applications are encouraged in the following areas:

- o Development of cloning techniques and strategies that improve upon current approaches to constructing physical maps;
- o Technology development to accelerate the assembly of the physical map of the mouse genome; and
- o Development of methods or strategies to address the problem of closure.

##### C. Resources

Many valuable resources have been developed for genetic and physical mapping projects. Therefore, in an effort to accelerate research in genetics and molecular biology and to eliminate unnecessary duplication of resources, the NCHGR is proposing to support activities in the area of genetic and physical mapping by encouraging applications that propose to develop such resources as:

- o A centralized gene mapping service for the scientific community; and
- o A centralized physical mapping service for the scientific community.

This list is not all-inclusive; identification of other resources that would accelerate research on mouse genetics and biology is encouraged.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by October 16, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows ICD staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

Letters of intent are to be sent to Dr. Bettie J. Graham at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted using the form PHS 398 (rev. 9/91). The RFA label available in the revised application kit MUST be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. Application kits are available in the business or grants office at most academic or research institutions, and from the Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441. Applications must be submitted by November 13, 1992.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by Division of Research Grants (DRG) staff for completeness and by NCHGR staff for responsiveness. Incomplete applications will be returned to the applicant without further consideration.

If the application is not responsive to the RFA, NCHGR staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by the Genome Research Review Committee (GRRC), NCHGR. Applications may be subjected to triage by the GRRC to determine scientific merit relative to other applications received in response to this RFA. The review criteria to be used are identified below. The NCHGR will withdraw from further competition those applications judged by triage to be noncompetitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will undergo further scientific merit review.

The second level of review will be conducted by the National Advisory Council for Human Genome Research.

#### AWARD CRITERIA

The following will be considered in making funding decisions: (1) quality of the proposed project as determined by peer review; (2) extent to which existing resources are utilized maximally; (3) value of the research for achieving the goals of the Human Genome Program with respect to the mouse genome; (4) adequacy of any plans proposed for managing data and sharing data and resources in a timely manner; (5) balance among projects with respect to the NCHGR current grant portfolio of mouse grants; and (6) availability of funds.

#### INQUIRIES

For more information regarding specific research areas or mechanisms and to obtain a copy of the complete RFA, please contact:

Bettie J. Graham, Ph.D.  
Chief, Research Grants Branch  
National Center for Human Genome Research  
Building 38A, Room 610  
Bethesda, MD 20892  
Telephone: (301) 496-7531  
E-mail: B2G@CU.NIH.GOV

For information about PHS Grant Policy, applicants may contact:

Ms. Alice Thomas  
Chief, Grants and Contracts Management Branch  
National Center for Human Genome Research  
Building 38A, Room 613  
Bethesda, MD 20892  
Telephone: (301) 402-0733

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.172. Awards will be made under the authority of the Public Health Service Act, Sections 301 (Public Law 78-410, as amended 42 U.S.C. 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirement of Executive Order 12372 or to Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### GENE REGULATION BY MEMBERS OF THE STEROID/THYROID SUPERFAMILY

NIH GUIDE, Volume 21, Number 26, July 17, 1992

PA NUMBER: PA-92-91

P.T. 34; K.W. 0765015, 0760085, 1002004, 1002008

National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute of Child Health and Human Development

#### PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Child Health and Human Development (NICHD) invite investigator-initiated research grant applications to study the molecular and cellular basis of hormonal regulation of gene expression by members of the steroid/thyroid hormone superfamily.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal

Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

The mechanism of support for this program will be the research project grant (R01).

#### RESEARCH OBJECTIVES

The purpose of this initiative is to stimulate research applications that will attempt to further characterize and define the roles of members of the steroid/thyroid hormone superfamily in the regulation of cell communication at the level of gene regulation. We envision this in the context of the regulation and integration of endocrine systems, as well as the pathogenesis, diagnosis, and therapy of disorders of endocrine systems. This includes questions of the linkage between mechanisms of signal transduction and change in expression of key genes and the involvement of hormone receptors, hormone response elements, and trans-acting factors in regulating the expression of specific genes in endocrine systems. Understanding the complete pathways involved in hormonal action will greatly further the knowledge of normal physiological function, development and disease.

#### Background

Numerous past contributions in endocrinology have served to define the basic nature of cell-cell endocrine communication resulting in changes in the behavior of those cells. Systemic release of "classical" hormones and hypothalamic peptides has been shown to define the physiological maintenance of homeostatic balance throughout the body. More recently, the emerging discipline of molecular endocrinology has identified diverse endocrine factors, including classically defined hormones that act to regulate intercellular (cell-to-cell) and intracellular (cell membrane-to-nucleus) communication through endocrine and paracrine or autocrine mechanisms. The ability of cells to respond to hormonal signals depends on the presence of specific cell surface and intracellular receptors, some of which are also responsible for direct chromosomal binding and subsequent modification of gene expression. In addition, it is now becoming clear that impairment in the ability of a hormone to bind to its cognate receptor or of that receptor to effectively signal the cell contributes to processes of disease development (e.g., development of benign endocrine neoplasias). It is also important to understand how the binding of hormone-receptor complexes to DNA is regulated, and how this binding signals the responsive genes to be expressed. At the level of individual cells, the effects of hormone action are often reflected in changes in the level and extent of gene expression. The recent explosion in knowledge of structures of known receptors for members of the steroid/thyroid hormone superfamily, including thyroid hormone, retinoids, vitamin D, glucocorticoids, sex steroids, and others for which ligands either do not exist or have not yet been defined (orphan receptors), has focused attention on a need for understanding the molecular mechanism(s) of action of these hormones. Therefore, current and future issues that need to be addressed relate to the precise sequence of events that translate hormone binding to cell surface and intracellular receptor(s) to such changes in cellular behavior, especially those resulting in changes in gene expression and focused on basic mechanisms of hormonal action.

#### Scope

Some examples of research topics that would be considered responsive to this solicitation include the following:

- o basic studies on the molecular and cellular basis of signal transduction
- o mechanisms of action of cell surface, intracellular, and/or intranuclear hormone receptors of the steroid/thyroid superfamily in effecting gene transcription
- o positive and/or negative hormonal response elements
- o the roles of receptors for these hormones/ligands as trans-acting factors involved in the expression of genes
- o cloning and expression of novel hormone receptors and identification of naturally occurring ligands for these receptors
- o identification and functional significance of genes whose expression is altered by specific hormones/ligands of the superfamily
- o identification of hormone receptors and/or related protooncogenes and their involvement in normal and abnormal cellular processes including disease development and progression
- o identification and characterization of accessory proteins that coregulate binding of ligand to receptor or that mediate signal transduction

These areas of interest are not listed in any order or priority, but emphasize general principles of endocrinology. They are only suggested examples of areas of research. Applicants are encouraged to propose other areas that are related to the objectives and scope describe above.

#### STUDY POPULATIONS

It is the NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them, and the study design must seek to identify any pertinent gender or minority population differences.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size



appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Item 4 (Research Design and Methods) of the Research Plan AND summarized in Item 5, Human Subjects. Applicants/offers are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit.

Application kits are available at most institutional business and grant/contract offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The number (PA-92-91) and title (Gene Regulation by Members of the Steroid/Thyroid Superfamily) of this announcement must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be assigned to Initial Review Groups for review and to Institutes or Centers for possible funding on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by Initial Review Groups of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by an appropriate Institute/Center national advisory council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that Institute or Center. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Ronald N. Margolis, Ph.D.  
Director, Molecular Endocrinology Research Program  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 621  
Bethesda, MD 20892  
Telephone: (301) 496-7504

Michael E. McClure, M.D.  
Reproductive Sciences Branch  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 603  
Bethesda, MD 20892  
Telephone: (301) 496-6515

Direct inquiries regarding fiscal matters to:

Sharon Tempchin  
Grants Management Specialist  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649D  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.847 (Diabetes, Endocrinology and Metabolic Diseases) and 93.864 (Population Research). Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SHORT-TERM INSTITUTIONAL NATIONAL RESEARCH SERVICE AWARDS

NIH GUIDE, Volume 21, Number 26, July 17, 1992

PA AVAILABLE: PA-92-92

P.T. 44; K.W. 0720005, 0404003, 0404009, 0715129

National Institute on Alcohol Abuse and Alcoholism  
National Institute on Drug Abuse  
National Institute of Mental Health

#### PURPOSE

The National Institute on Alcohol Abuse and Alcoholism, National Institute on Drug Abuse, and National Institute of Mental Health provide short-term (three months or less) National Research Service Awards (NRSAs) to eligible institutions to develop or enhance research training opportunities for individuals who are interested in careers in specified areas of biomedical and behavioral research.

Each institute has different program goals and initiatives; therefore, potential applicants must contact the appropriate institute office listed below, prior to preparing an application, to obtain the full Program Announcement and current information about the institute's interests with regard to short-term NRSAs.

#### ELIGIBILITY REQUIREMENTS

Domestic, public and private nonprofit institutions and professional organizations may apply. The applicant institution must have the staff and facilities to conduct the proposed research training in a suitable environment for performing high-quality work.

Individuals receiving support under individual or other institutional NRSA training grants are not to be appointed to short-term positions. Trainees in short-term training programs are not immediately subject to the NRSA requirement for payback (please see the full Program Announcement for an explanation of the payback requirement).

**Trainee Requirements:** Individuals selected to be recipients of Short-Term Institutional NRSA trainee positions must be citizens or noncitizen nationals of the United States, or have been lawfully admitted to the United States for permanent residence and have in their possession an Alien Registration Receipt Card (I-151 or I-551) at the time of appointment to the training program. Predoctoral applicants must have received a baccalaureate degree and be enrolled in a doctoral degree program at the time of appointment. Postdoctoral individuals selected to receive short-term NRSA traineeships must have received a Ph.D., Psy.D., M.D., D.D.S., D.N.S., D.S.W., Pharm.D., or equivalent domestic or foreign degree from an accredited institution as of the date of appointment. Certification by an authorized official of the degree-granting institution that all degree requirements have been met is also acceptable.

#### MECHANISM OF SUPPORT

The mechanism of support is the Short-term Institutional NRSA (T35). Short-term training grants are intended for pre-doctoral students, medical students, postdoctoral students, residents interested in pursuing research careers, and research scientists. Short-term training support is not intended, and may not be used, to support activities that would ordinarily be part of a research degree program.

The training program director at the institution will be responsible for selection and appointment of individuals to receive Short-Term Institutional NRSA support and for the overall direction of the research training program. The training program must provide opportunities for individual trainees with the primary objective of extending their skills and knowledge in preparation for a research career. Special attention should be given to the appointment of minorities and women.

NRSAs are not made for study leading to the M.D., D.O., D.D.S., or other similar professional degrees, nor do they

support residency training. Successful trainees may be reappointed for a different/continuing course of training (not to exceed two reappointments), and, when appropriate, encouraged to pursue appointment to a standard research training program.

**Period of Support:** Awards for institutional grants may be made for project periods of up to five years. By law, an individual may receive no more than five years of support in the aggregate at the predoctoral level and three years of support in the aggregate at the postdoctoral level under the NRSA program, including any combination of support from individual and institutional awards.

**Stipends and Related Costs:** Stipends will be based on a monthly proration (not to exceed a three month period) of the annual stipend level. The annual stipend for predoctoral individuals at all levels is \$8,800; therefore, the monthly stipend will be \$734.

For postdoctoral individuals, the annual stipend is determined on the basis of the number of years of prior relevant postdoctoral experience. This determination is made at the time of each appointment or reappointment of an individual.

The Tax Reform Act of 1986, Public Law 99-514, describes the tax liability of all individuals supported under the NRSA program.

The institution may request up to \$125 per month per predoctoral individual and \$208 per month per postdoctoral individual to offset the cost of tuition, fees, supplies, certain types of travel for trainees, and other expenses; and actual indirect costs or eight percent of allowable direct costs (whichever is less) to cover related institutional overhead. Tuition at the postdoctoral level is limited to that required for specified courses in support of the approved training program, not to exceed \$208 per month. Applicants may request additional trainee-related expenses if the nature of the program requires exceptional support.

#### RESEARCH OBJECTIVES

The proposed training should be in select, focussed, often emerging, scientific areas relevant to the mission of the funding institute that encompass concepts and methods of the relevant disciplines, including basic and clinical sciences, and that are of sufficient depth to enable the trainees, upon completion of the program, to have a thorough exposure to the principles underlying the conduct of research. Applicants for short-term research training grants should propose a well-integrated program that involves intensive training in a closely supervised environment.

Every application must include the following information about the training program:

- o All new research training grant applications are required to have a plan for recruitment of minority trainees, including a description of specific steps to be taken for recruitment and retention. Competing renewal applications are required to include a list of accomplishments in recruitment, retention, and progress of minority students achieved in the prior project period in addition to plans for recruiting minority trainees in the next project period. Competing applications without a minority recruitment plan and/or a report of accomplishments in recruiting minority trainees will not be reviewed until these items are received.
- o All competing applications must include evidence that the principles of responsible scientific conduct will be incorporated in the research training experience of each trainee. Applications without plans to provide such instruction will not be reviewed until a plan is received.
- o Applications must include discussion of the relevance of the proposed short-term training program to specific research programs at the funding institute.

#### SPECIAL REQUIREMENTS

Before a trainee can be appointed to an NRSA institutional grant and receive an NRSA under the grant, he or she must meet NRSA eligibility requirements. Institutions shall notify prospective trainees of these provisions prior to or at the time an appointment is offered. The Payback Agreement Form must be completed and submitted to the awarding institute immediately upon appointment of a new trainee.

**Payback Requirement:** Since the time spent in short-term research training will usually total less than 12 months, short-term trainees will usually have no service payback obligation from this specific short-term support. The time spent on NRSA support is accrued, however, along with any future NRSA support in calculating the total service obligation. This obligation requires that any NRSA support in excess of 12 months be repaid by an equal period of health-related research or health-related teaching. Activities carried out while supported by NRSAs may not be used to fulfill the payback requirements.

The institution must submit to the funding institute a Statement of Appointment form (PHS 2271, revision 10/91) and a Payback Agreement Form (Form PHS 6031, revision 10/91) each time a trainee is appointed or reappointed to the grant. At the end of each appointment, a Termination Notice (Form PHS 416-7, revision 10/91) must be completed and returned to the institute.

Trainees are required to pursue research training on a full-time basis, devoting at least 40 hours per week as specified by the sponsoring institution in accordance with its policies. An NRSA may not be held concurrently with another Federally sponsored fellowship or similar Federal award that provides a stipend or otherwise duplicates provisions of the NRSA. An awardee may, however, accept concurrent educational remuneration from the Veterans Administration and loans from Federal funds.

#### APPLICATION PROCEDURES

Applicants for Short-Term Institutional NRSAs must use and follow the instructions accompanying the Grant Application Form PHS 398 (rev. 9/91), which contains special instructions for institutional NRSAs. These forms

are available from institutional offices of sponsored research or their equivalent. If not available locally, they may be obtained from the offices listed at the end of this announcement. The title and number of this Program Announcement, Short-term Institutional National Research Service Awards (PA-92-92) must be typed in Item 2a on the face page of the application form. Applications will be accepted at these receipt dates: January 10, May 10, and September 10. Applications received after these receipt dates are subject to assignment to the next review cycle or may be returned to the applicant.

Eligible institutions desiring to request support under this program are encouraged to review the research areas specified in the Attachment to the Program Announcement. The complete Program Announcement and the Attachment are available from the offices listed below.

#### REVIEW CONSIDERATIONS

Short-Term Institutional NRSA training grant applications are reviewed for scientific and educational merit by institute initial review groups composed primarily of nongovernment scientists and are also subject to the review and recommendations of the appropriate National Advisory Council.

Major considerations in the review are the following: the qualifications of participating faculty, their success in previous training endeavors, and the relevance of the training program to institute research programs; the breadth, depth, and quality of the training program; the plans for recruiting and selecting trainees; and the adequacy of the training facilities and resources. Detailed review criteria are listed in the full Program Announcement.

#### AWARD CRITERIA

Awarding components select applications for funding primarily on the basis of scientific merit review results, but other factors may be considered such as: availability of funds, research program priorities, balance among types of research training supported by the awarding component, and minority recruitment efforts.

#### INQUIRIES

The full Program Announcement and Attachment, up-to-date policy guidelines, and the application forms may be obtained from any of the following offices:

National Institute on Alcohol Abuse and Alcoholism  
Office of Scientific Affairs  
5600 Fishers Lane, Room 16C20  
Rockville, MD 20857  
Telephone: (301) 443-4375

National Institute on Drug Abuse  
Office of Extramural Program Review  
5600 Fishers Lane, Room 10-42  
Rockville, MD 20857  
Telephone: (301) 443-2755

National Institute of Mental Health  
Division of Extramural Activities  
5600 Fishers Lane, Room 9-105  
Rockville, MD 20857  
Telephone: (301) 443-1596

Inquiries regarding grants management may be directed to:

Grants Awards and Operations Section  
Grants Management Branch  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C05  
Rockville, MD 20857  
Telephone: (301) 443-4414

#### AUTHORITY AND REGULATIONS

Awards will be made under the authority of Section 487 of the Public Health Service Act as amended (42 USC 288) and administered in accordance with the PHS Grants Policy Statement, revised October 1990.

#### REVISED NLM RESOURCE GRANT PROGRAM

NIH GUIDE, Volume 21, Number 26, July 17, 1992

PA NUMBER: PA-92-93

P.T. 34; K.W. 1004017, 1004008

National Library of Medicine

#### PURPOSE

The Resource Awards of the National Library of Medicine (NLM) assist health science libraries in improving services by the application of computer and telecommunication technology. The description of the program has been revised to clarify some ambiguities in the earlier description and to call attention to current NLM policies that reflect



the Long-Range Plan and recent initiatives of the Federal Government in the field of High Performance Computing and Communications (HPCC). Although the language is similar in general to the previous description, prospective applicants should note particularly the emphasis on on-line access, document delivery, use of NLM programs, sensitivity to the growing importance of information networks, and the review criteria.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement, Revised National Library of Medicine Resource Grant Program, is related to the priority area of educational and community based programs. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications for resource grants may be made by any domestic public or private, nonprofit health science institution or organization. Health science institutions include, but are not limited to, schools of the health professions, health-related research institutions, health professional associations, and health care institutions, including hospitals, and other agencies of State and local governments. Participants in consortium/contractual arrangements may be any organizational entity (including, for example, Federal institutions, proprietary hospitals, and public libraries) that will significantly contribute to the service improvement objectives of the whole project. Women and minority applicants, in particular, are encouraged to apply. Foreign institutions are not eligible for Medical Library Resource (G07 and G08) Awards.

## MECHANISM OF SUPPORT

The primary mechanisms of support under this Program Announcement are the medical library information access grant (G07) and the medical library information systems grant (G08). The grant mechanisms only fund direct costs.

## OBJECTIVES

The Long-Range Plan of the NLM states that opportunities for progressing from the present to the "electronic world of the future" are linked to improving the infrastructure for information transfer and facilitating the effective use of this infrastructure. The Plan also emphasizes the importance of providing medical libraries with access to national networks. It is appropriate that the resource grant mechanism concentrate its efforts on an area of need also identified by Congress in 1964 in the premier Medical Library Assistance Act: the use and improvement of technology necessary to coordinate and disseminate health science information.

A new emphasis on technology and technological systems as the primary means to meet broad Resource Program objectives has fundamental applicability to both types of awards.

In addition, both award types hope to encourage, where feasible, consortium/contractual arrangements that foster the sharing or expanded accessibility of information resources. Lastly, because high-performance national networks will surely be the "information highways" of the future, the NLM wishes to encourage strongly applications that incorporate as an essential feature on-line access to NLM databases by institutions or by individual users. Applications that do not incorporate national network access, such as applications to purchase CD-ROM systems, for example, will not normally be funded.

Successful applicants will be those who communicate an understanding that Resource Awards are not merely grants for hardware or telecommunication systems. Most likely to be favorably received are applications for systems capable of expediting the flow of information to end-users; accordingly, applicants are also asked to consider ways and means of increasing use of the proposed system by health professionals through training and/or cooperation with medical directors and professional societies, or some other technique.

Particularly welcome will be applications that utilize NLM programs such as GRATEFUL MED, DOCLINE, LONESOME DOC, and other NLM databases that carry out the objectives of the OUTREACH initiative. Connection to Internet is strongly encouraged whenever local circumstances permit. The NLM has a strong interest in participating in the National Research and Education Network (NREN), which is now under active development with the support of the Federal Government. The NLM believes that NREN, which will build on the existing Internet, will be the principal biomedical information communications system in the years to come.

The NLM has a special interest in applications that support its outreach program by improving information availability in underserved rural and inner-city health care facilities.

The focus is different for each of the two award types.

### o The Information Access Grant

The purpose of the Information Access Grant is to facilitate access to and delivery of health science information through up-to-date computer and telecommunication technology. Access Projects should promote a dynamic link between health professionals and relevant information resources. On-line access to NLM databases and/or some provision for providing documents should be elements of the application.

Information Access Awards are primarily directed to the libraries of small to medium-sized community hospitals where the need for short-term assistance to achieve these objectives is most evident. If the application proposes to promote searching of databases by individuals, appropriate attention should be given to training users to accept and utilize the proposed technology.

Single institutions may apply for up to \$12,000 for one year of support. Applications involving consortium/contractual arrangements may be for up to \$12,000 for one year for each participating institution and, as an option,

the responsible applicant institution may include a request for \$12,000 for an initial year for planning and organizing the consortium. Although the one-year planning award and one-year implementation phase are requested concurrently in the initial application, the funding of the second (implementation) year will be contingent on the progress made and the quality of the plans developed. Existing consortia may not need this optional year; however, the formal agreement(s) or contract(s) requested by the application instructions must address the programmatic, fiscal, and administrative arrangements between the applicant and the collaborating organizations in the context of the Information Access Project. Some institutions may lack appropriate staffing to design and implement a competitive application or may need technical advice. In such cases, the regional medical library of the applicant may be of assistance, and appropriate consultation may be budgeted.

#### o The Information Systems Grant

The Information System Grant, like the Information Access Grant, is intended to facilitate the utilization of health science information. It is distinguished from the Access award by the scope and nature of the technological means utilized. It may encompass whole systems or it may seek to establish connectivity of system components. The Information Systems Grant also provides support for innovative improvements to the infrastructure, for example, using an artificial intelligence technique as a strategic asset for managing information. Information Systems Grants are primarily directed to academic health science institutions and larger hospitals with significant teaching and research components. The organizational unit within the institution that is directly responsible for the conduct of the project may be the library or other information service/research-related department. However, the grant is not a research instrument and the project must be for an operational service activity. Applicants for Systems Grants are urged to incorporate on-line access to NLM databases and some provision for document delivery into their applications.

Information Systems Grants may be for a one- to three-year period and, except in unusual circumstances, are not renewable. Based on the availability of appropriated funds, the range of awards will be approximately \$50,000 to \$150,000 per year.

Pre-application planning is essential for a well-written but in most instances can be carried out by existing institutional mechanisms. However, just as the Information Access Grant provides an NLM-supported planning period for consortium organization and development, certain Information Systems application (e.g., an inter-institutional project for comprehensive computer networking) might also justify short-term planning assistance from NLM. A twelve-month or less separate planning award for a subsequent Information Systems project is allowable. Such planning assistance is primarily for multi-institutional projects for which the support could be a unifying and persuasive catalyst. The support is intended to defray costs such as meeting and travel expenses, legal (contract) fees, staff release time for surveys of technological resources, and consultant fees for assessment of systems compatibility.

#### APPLICATION PROCEDURES

Applicants are to use the research grant application form PHS 398 (rev. 9/91), available at the applicant's institutional Application Control Office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 240, Bethesda, MD 20892, telephone (301) 496-7441.

Complete item 2a on the face page of the application indicating that the application is in response to this Program Announcement and print (next to the checked box) REVISED NLM RESOURCE GRANT PROGRAM.

The application and five copies must be mailed or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Additional information and assistance are available from the National Library of Medicine, telephone (301) 496-4221, FAX (301) 402-0421; and are also available from the Regional Medical Libraries. Deadline dates for all new applications are: February 1, June 1, and October 1.

#### REVIEW CONSIDERATIONS

Applications will be reviewed for merit by the Biomedical Library Review Committee. Following initial review, the applications will receive a second-level review by the Board of Regents of the National Library of Medicine.

Applicants should verify that each of the following critical review elements is adequately addressed in the appropriate parts of the application or its appendices:

- o Appropriateness of project (objectives vs. information needs of users)
- o Feasibility of objectives
- o Appropriate use of technology (including user training)
- o Qualifications and experience of key personnel
- o Plan for estimating the achievements of the proposed project
- o Assurance of communication of results (see SPECIAL REQUIREMENTS above)
- o Appropriateness of grant budget and likelihood that applicant will continue support of project after the grant period
- o Conformity to the spirit of the NLM Long-Range Plan as described in this Program Announcement

Institutions applying for resource grants should recognize that even moderately successful projects will generate additional institutional expenses during and after the period of NLM grant support. Assurance that such costs will be covered by the institution is given, tacitly, by the acceptance of an award. It is important that reviewers are persuaded that adequate attention has been given to fiscal planning and that post-award fiscal commitments are sound.

## AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to the NLM. The following will be considered when making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Applicants are encouraged to contact:

Mrs. Frances E. Johnson  
Biomedical Information Support Branch  
Extramural Programs  
National Library of Medicine  
Building 38A, Room 5S520  
Bethesda, MD 20894  
Telephone: (301) 496-4221

Application materials and information may also be obtained from the Regional Medical Libraries of the National Network of Libraries of Medicine (NN/LM), a list of which is available from Mrs. Johnson.

Direct inquiries regarding fiscal matters to:

Ms. Ellen Meltzer  
Grants Management Specialist  
National Library of Medicine  
Building 38A, Room 5N515  
Bethesda, MD 20894  
Telephone: (301) 496-4253

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance under Medical Library Assistance, Chapter 93.879. Grants will be awarded under the Authority of the Public Health Service Act, Section 474(42 USC 286b-5) and administered under PHS grants policies and Federal Regulations, most specifically at 42 CFR Part 59a and 45 CFR part 74. This program is not subject to the intergovernmental review requirements of Executive order 12372 or Health Systems Agency review.

## CENTERS FOR RESEARCH ON SERVICES FOR PEOPLE WITH SEVERE MENTAL DISORDERS

NIH GUIDE, Volume 21, Number 26, July 17, 1992

PA AVAILABLE: PA-92-94

P.T. 04; K.W. 0730050, 0715129

National Institute of Mental Health

## PURPOSE

The National Institute of Mental Health (NIMH) announces the availability of support for Centers for Research on Services for People with Severe Mental Disorders. The purpose of these Centers is to promote, develop, and conduct multidisciplinary research to improve the organization, financing, delivery, quality, effectiveness, and outcomes of mental health services for persons with severe and persistent mental disorders.

This Program Announcement addresses one of the major recommendations set forth in Caring for People with Severe Mental Disorders: A National Plan of Research to Improve Services. Potential applicants may obtain a copy of Caring for People with Severe Mental Disorders (Department of Health and Human Services Pub. No. (ADM)91-1762) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238). It also complements the NIMH PA-92-65, Implementation of Caring for People with Severe Mental Disorders: A National Plan of Research to Improve Services, which invites applications for research project grants, research demonstrations, and career development applications in support of this National Plan, NIH Guide for Grants and Contracts, Vol. 21, No. 12, April 3, 1992. Copies of PA-92-65 may be obtained from the National Institute of Mental Health, Room 9-95, 5600 Fishers Lane, Rockville MD 20857; telephone 301-443-4673.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Centers for Research on Services for People with Severe Mental Disorders, is related to the following objectives set forth in "Healthy People 2000: National Health Promotion and Disease Prevention Objectives:" Objective 6.4, reduce the prevalence of mental disorders among adults living in the community to less than 10.7 percent; Objective 6.6, increase to at least 30 percent the proportion of people aged 18 and older with severe, persistent mental disorders who use community support programs; Objective 6.7, increase to at least 45 percent the proportion of people with major depressive disorders who obtain treatment; Objective 6.8, increase to at least 20 percent the proportion of people aged 18 and older who seek help in coping with personal and emotional problems; and Objective 6.12, establish mutual help clearinghouses in at least 25 States. Potential applicants may obtain a copy of "Healthy People 2000" (Full



#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This PA will use the National Institutes of Health (NIH) Specialized Center (P50) mechanism. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present PA may not exceed five years.

#### Terms and Conditions of Support

Grant funds may be used for expenses clearly related and necessary to conduct the proposed Center, including direct costs and allowable indirect costs. Grant funds may not be used to operate a treatment, rehabilitation, or other service program. Support may be requested for a period of up to five years.

Funds may be requested for core support of the Center and for research core areas. Core support costs may include salaries of core personnel, including the Center Director, and research resources to be shared across projects, such as statistical consultation, data analysis, and storage systems, and equipment. Funds from the Center grant may not be used to support service costs incurred in carrying out research; these funds must be sought from other sources.

#### Period of Support

Applications may request support for up to five years. Annual awards will be made, subject to continued availability of funds and progress achieved.

#### FUNDS AVAILABLE

The funding cap for a Center for Research on Services for People with Severe Mental Illness is \$500,000 per year, plus negotiated institutional indirect costs. Applications requesting direct costs in excess of this amount will be returned to the applicant without review.

It is anticipated that up to three new awards may be made in FY 93. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the Institute, awards pursuant to this PA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

Millions of Americans suffer from severe, persistent, and disabling mental disorders that can devastate their lives and the lives of those around them. The nature of these illnesses is such that those who suffer from them often have pervasive difficulty maintaining good physical health, coping with the tasks of daily living, finding and retaining work, fulfilling homemaking responsibilities, and forming and sustaining social relationships.

Because severe mental illnesses are associated with disturbances in thinking and behavior, these disorders have been the subject of much misunderstanding in the past. Fortunately, there is now widespread recognition that mental illnesses are true illnesses. As in the case of physical illnesses, it is possible through research to develop improved treatments and services that can attend more effectively to the needs that persons with severe mental illness have for medical treatment and to their care, social support, rehabilitation, housing, and enhanced quality of life.

Mental health services research is still an underdeveloped field. To focus attention on this problem and develop a remedial strategy, NIMH convened three panels of experts to prepare Caring for People with Severe Mental Disorders: A National Plan of Research to Improve Services. The Clinical Services Research Panel considered areas ranging from diagnosis to outcome assessment, with a major focus on improving the quality of clinical care and evaluating the impact of clinical services. The Service Systems Research Panel focused on structures and processes of mental health service delivery, ranging from the organization and financing of services to legal issues and society's attitudes towards the mentally ill. The Research Resources Panel addressed the infrastructure needed to implement the substantive recommendations of the other two panels.

This announcement responds to a recommendation of the Research Resources Panel that NIMH expand and increase its support for multidisciplinary mental health services research centers. These centers are needed to provide stimulating and productive environments in which investigators from fields of services research, clinical science, economics, public health, and behavioral and sociocultural science can interact and direct their energies toward the conceptualization and development of studies to improve services for persons with severe mental illness.

In keeping with the scope of the national plan which this announcement is intended to help implement, applications submitted in response to this announcement should focus their proposed research on services for adult (including elderly) persons with severe mental disorders. Although some limited support may be requested under this announcement for research on children and adolescents, support for services research in this area is available under two other NIMH program announcements. For greater detail on the specifics of funding for child and adolescent mental health services research, applicants should refer to the NIMH PAs Implementation of the National Plan for Research on Child and Adolescent Mental Disorders (PA-91-46), April 1991, which solicits research grant applications to expand the full spectrum of research related to child and adolescent mental disorders, and Centers for Research on Mental Health Services for Children and Adolescents (PA-92-22), which solicits center grant applications to



develop multidisciplinary research that can help to improve the organization, financing, delivery, effectiveness, and outcomes of mental health services for children and adolescents. Copies can be obtained from the National Institute of Mental Health, Room 9-95, 5600 Fishers Lane, Rockville MD 20857, telephone 301-443-4673.

#### APPLICATION PROCEDURES

Applicants are to use the Public Health Service research grant application form PHS 398 (rev. 9/91). These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441; and from Grants Management Branch, National Institute of Mental Health, 5600 Fishers Lane, Room 7C-05, Rockville, MD 20857, telephone 301-443-4414.

Applications will be reviewed once a year according to the following review schedule: receipt date of a new application, October 1; receipt date of a competing continuation, supplemental, or revised application, November 1; initial review, February/March; Advisory Council review, May/June; earliest start date, July 1. Applications received after the given receipt date will be returned to the applicant without review.

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by an initial review group (IRG) of a funding component composed primarily of non-Federal scientific experts. Final review is by the appropriate National Advisory Council; review by Council may be based on policy considerations as well as scientific merit. Only applications recommended for consideration for funding by the Council may be supported. Summaries of IRG discussions are sent to applicants as soon as possible following IRG review.

Criteria for scientific/technical merit review of Center applications are contained in the full Program Announcement.

#### AWARD CRITERIA

Preference will be given to projects consistent with the NIMH Public-Academic Liaison initiative (bringing together public sector service providers and academic researchers) and to projects involving special populations (e.g., minorities, women, those living in rural areas, impoverished and homeless persons).

Factors considered in determining which applications will be supported include quality as determined by IRG and Council recommendations, program needs and priorities, and availability of funds.

#### INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome, and NIMH staff are available for consultation in advance of or during the process of preparing an application. Potential applicants should contact NIMH as early as possible for information and assistance in initiating the application process and developing an application.

Inquiries and requests for the full PA may be directed to:

Thomas L. Lalley, M.A., Chief  
or  
Kathryn M. Magruder, M.P.H., Ph.D., Assistant Chief  
Services Research Branch  
Division of Applied and Services Research  
National Institute of Mental Health  
Parklawn Building, Room 18C-14  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-3364

For further information on grants management issues, applicants may contact:

Stephen J. Hudak  
Chief, Grants Management Section  
National Institute of Mental Health  
Parklawn Building, Room 7C-23  
5600 Fishers Lane  
Rockville MD 20857  
Telephone: (301) 443-4456

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance 93.242, Mental Health Research Grants. Grants must be administered in accordance with the PHS Grants Policy Statement (Rev. October 1990). Federal Regulations at 42 CFR Part 52, "Grants for Research Projects," and 45 CFR Parts 74 and 92 concerning administration of grants, are applicable to these awards. This PA is not subject to the intergovernmental review requirements of Executive Order 12372, as implemented through DHHS regulations at 45 CFR Part 100.

CLINICAL RESEARCH ON HUMAN DEVELOPMENT

NIH GUIDE, Volume 21, Number 26, July 17, 1992

PA NUMBER: PA-92-58

P.T. 34; K.W. 0404009, 0775025, 0755020

National Institute on Drug Abuse



The National Institute on Drug Abuse, Alcohol, Mental Health and Drug Abuse Administration, wishes to amend program announcement PA-92-58 published in the NIH Guide for Grants and Contracts, Volume 21, Number 12, March 27, 1992, to add to the Areas of Interest the following section:

o Studies of Community-Based Research Interventions for Children of Drug Abusing Parents

Studies are needed to evaluate the efficacy of community-based interventions for children ages 3 to 12 years who show evidence of behavior disorders or the potential for developing behavior disorders in association with parental drug abuse and/or being raised in a household in which drugs have been prevalent. Some examples of interventions are: (1) model programs for foster care (including kinship care) in which the child has been officially adjudicated into the foster care system or placed in the home of relatives; (2) model programs for children who are known to local child protective service agencies that are responsible for administering child abuse/neglect services or related child abuse/neglect intervention services; and (3) model programs for children of drug abusers whose parents are enrolled in a drug treatment program. This is not an exhaustive list. The applicant should describe how she or he will have access to the target population and assure the appropriate numbers for sampling. The applicant will be responsible for describing the hypotheses to be tested utilizing experimental and control comparisons. Interventions may include: (a) innovative strategies that have been used, but have not been tested previously in research studies; or (b) innovative strategies that have not been previously developed. All interventions must be culturally sensitive to the target population. As needed, applicants are encouraged to form a coalition with appropriate public and/or private community agencies to plan and carry out the grant studies. A variety of interventions may be appropriate. These include, but are not limited to: (a) comprehensive service delivery approach; (b) the use of specialized multidisciplinary teams; (c) parenting skills programs; (d) home visiting models; (e) specialized interventions coordinated through the schools; (f) innovative group, family or individual counseling; (g) innovative group home/foster care strategies, and (h) innovative case management systems. It should be noted that dollars for service delivery can be supported only for service delivery in support of the research.

For further information and consultation on this program area, applicants may contact:

Rebecca S. Ashery, D.S.W.  
Community Research Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 9A-30  
Rockville, MD 20857  
Telephone: (301) 443-6720

RESEARCH SUPPLEMENTS TO PROMOTE REENTRY INTO BIOMEDICAL AND BEHAVIORAL RESEARCH CAREERS

NIH GUIDE, Volume 21, Number 26, July 17, 1992

P.T. 34, II; K.W. 0710030, 1014006

National Institutes of Health

This announcement that appeared in the NIH Guide for Grants and Contracts, Vol. 21, No. 25, July 10, 1992, contained an incorrect address for the National Institute on Aging. The following is the correct address:

NATIONAL INSTITUTE ON AGING

Deputy Associate Director  
Office of Extramural Affairs  
Gateway Building, Room 2C218  
Bethesda, MD 20892  
Telephone: (301) 496-9322

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816

THE NIH GUIDE WILL NOT BE PUBLISHED ON JULY 24, 1992. THE NEXT ISSUE OF THE NIH GUIDE WILL BE ON JULY 31, 1992.

# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 27  
July 31, 1992

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES

NIH AIDS LOAN REPAYMENT PROGRAM FOR RESEARCH

NIH GUIDE, Volume 21, Number 27, July 31, 1992

P.T. 23; K.W. 0715008, 1014006

National Institutes of Health

PURPOSE

This notice is a republication, with minor modifications, of the April 10, 1992 (NIH Guide for Grants and Contracts, Vol. 21, No. 14), issuance on this subject. It is being reissued for informational purposes and to emphasize the availability of this program.

On November 4, 1988, the United States Congress enacted Public Law 100-607, directing the National Institutes of Health (NIH) to establish a program of educational loan repayment to attract additional investigators into Acquired Immunodeficiency Syndrome (AIDS) research. The NIH Loan Repayment Program for AIDS Research (LRP), in order to increase the number of investigators conducting AIDS research at the NIH, invites interested health professionals to apply for LRP participation.

The LRP may pay a maximum of \$20,000 a year directly to a participant's lenders for qualifying educational debt during an initial, minimum two-year service period. The actual loan repayment is based, in part, on the availability of funding as well as the proportion of the participant's qualifying debt relative to their NIH basic pay or stipend. Since such payments to lenders are considered income for the participant and increases his/her Federal tax liability, the LRP also makes payments, equal to 39 percent of the total loan repayments, directly towards the participant's Internal Revenue Service (IRS) account. The LRP may make additional tax reimbursements to those participants who show an increase in State and/or local tax liability. Benefits are paid in addition to a participant's annual NIH basic pay or stipend.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This announcement, NIH AIDS Loan Repayment Program for Research, is a program that is related to the priority area of HIV infection. Those interested may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

An applicant to the LRP is accepted for LRP participation when his/her qualified AIDS research assignment is approved by the AIDS Research Loan Repayment Advisory Committee (LRAC) and his/her contract is executed. Specific LRP applicant and participant eligibility criteria include the following:

- (1) Applicants must be citizens or permanent residents of the United States;
- (2) Applicants must have a Ph.D., M.D., D.O., D.D.S., D.M.D., D.V.M., or equivalent degree;
- (3) Applicants must have qualified educational debt in excess of 20 percent of their annual NIH basic pay or stipend on the date of program eligibility, resulting from governmental or commercial loans obtained to support their undergraduate and/or graduate education;
- (4) Individuals who are not NIH employees, such as Visiting Fellows, Intramural Research Training Award (IRTA) recipients, National Research Service Award (NRSA) recipients, Guest Researchers or Special Volunteers, NIH National Research Council (NRC) Biotechnology Research Associates Program participants, and Intergovernmental Personnel Act (IPA) participants, may NOT participate in the LRP;
- (5) Individuals employed by the NIH during the period November 4, 1987, through November 3, 1988, are INELIGIBLE;
- (6) Applicants may be appointed under a temporary or permanent employment mechanism, as long as their employment with the NIH has the potential to last a minimum of two years;
- (7) Individuals with existing service obligations to Federal, State, or other entities will NOT be considered for the LRP unless deferrals are granted for the length of the LRP service obligation; and
- (8) Applicants will NOT be excluded from consideration under the LRP on the basis of race, color, creed, religion, sex, handicap, age, national origin, or political affiliation.

In addition, in order to qualify for repayment, LRP applicants' debts are subject to the following limitations and restrictions:

The LRP will repay lenders for the principal, interest, and related expenses (such as the required insurance premiums on the unpaid balances of some loans) of qualified Government (Federal, State, and local) and commercial educational loans obtained by participants for the following: (1) undergraduate, graduate, and health professional school tuition expenses; (2) other reasonable educational expenses required by the school(s) attended, including fees, books, supplies, educational equipment and materials, and laboratory expenses; and (3) reasonable living expenses, including the cost of room and board, transportation and commuting costs, and other reasonable living expenses as determined by the LRP.

The following loans are NOT repayable under the LRP: (1) loans not obtained from a Government entity or commercial lending institution, such as loans from friends, relatives, or other private individuals; (2) loans for which contemporaneous documentation is not available; (3) loans or portions of loans obtained for educational or living expenses that exceed the "reasonable" level as determined by the standard school budget for the year in which the loan was made, and are not determined by the LRP to be reasonable based on additional documentation provided by the applicant; and (4) loans, financial debts, and service obligations incurred under the Physicians Shortage Area Scholarship Program, National Research Service Award Program, Public Health and National Health Service Corps Scholarship Training Program, National Health Service Corps Scholarship Program, Armed Forces (Army, Navy, or Air Force) Health Professions Scholarship Program, and Indian Health Service Scholarship Program.

Loans in default, or loans not current on payment schedule, will not be considered as qualifying for repayment. Repayments will only be made for loans with current payment status. During lapses in loan repayments, due either to program administrative complications or a break in service, participants are wholly responsible for

making payments or any other arrangements that maintain loans in a current payment status. Penalties assessed to participants as a result of LRP administrative failures to maintain current payment status may be considered for reimbursement.

Payments will NOT be made under the LRP for loans that participants have paid prior to the program eligibility date.

#### RESEARCH OBJECTIVES

The LRP is designed to attract additional investigators into AIDS research. The LRP intends to fund individuals conducting AIDS research as described in the following paragraphs that contain the "Activities Constituting AIDS Research" criteria as adopted by the LRAC on September 20, 1991:

"The following parameters define whether a proposed research assignment meets the criteria for coverage under the NIH AIDS Research Loan Repayment Program - that is, whether the incumbent will be "primarily" engaged in AIDS research. "Primarily" engaged in AIDS research is defined as AIDS research activities that constitute at least 80 percent of a researchers time. Clinical Associates, whose intent is to primarily engage in AIDS research, must engage in qualified AIDS research for at least 3 months in the first year of the program, with a total of 15 months of qualified AIDS research during their 2-year contract.

"AIDS research includes studies of the human immunodeficiency virus (HIV), the pathophysiology of HIV infection, the development of models of HIV infection and its sequelae, cofactors predisposing to HIV infection and AIDS, or its sequelae, and the development of vaccines and therapeutics. More specifically, the following research activities are included: (1) studies of HIV and related retroviruses; (2) studies of the mechanism(s) by which HIV and related retroviruses establish infection and infect host cells; (3) studies of the mechanism(s) by which HIV and related retroviruses cause disease, including studies of the immune deficiency induced by HIV and related retroviruses; (4) studies of the pathophysiology of host response to HIV infection; (5) studies of in vivo and in vitro models of human HIV infection and its sequelae; (6) epidemiologic studies of HIV and related retrovirus infection; (7) clinical trials involving prophylaxis or therapy for HIV infection or its sequelae; (8) preclinical studies aimed at the development of therapy for or prevention of HIV infection and the immunodeficiency caused by HIV infection and its sequelae; (9) cofactors predisposing to acquiring HIV infection; (10) basic studies and clinical trials involving vaccines and other immunological or chemotherapeutic interventions for the prevention of HIV infection and its sequelae; and (11) basic studies into the transmission of HIV involving high-risk behaviors and research concerning the interruption of transmission by behavioral change and pharmacologic intervention.

"AIDS researchers include scientists who are intellectually engaged in the process of providing scientific direction and guidance in programs of original AIDS research, specifically epidemiologists, statisticians, and others who are involved in the design and conduct of research studies. The duties of such scientists may include the generation and design of studies, the collation and analysis of data, and/or the preparation and publication, as author or co-author, of studies in peer-reviewed journals. AIDS researchers also include physicians who are providing care for HIV-infected individuals who are subjects of HIV-related research."

#### APPLICATION PROCEDURES

Individuals wishing to apply to the LRP must first obtain a firm employment commitment from an Institute, Center, or Division (ICD) Personnel Department. An initiating official, who may be a laboratory or branch chief, must recommend an individual for application to the LRP, and the ICD Scientific Program Director and ICD Director must concur. LRP participation is contingent, in part, upon employment with the NIH, and candidates may not be recommended for loan repayment by an ICD until a firm employment commitment has been made by the recommending ICDs Personnel Department.

Applicants must submit a signed contract, along with the completed LRP application package, to be considered for participation in the program.

At the conclusion of the initial contract, participants may reapply and be considered for subsequent, one-year continuation contracts. Continuation contracts are based upon the same review criteria as the initial contract, in addition to a description of AIDS research accomplishments made during the initial contract. These continuation contracts are approved on a year-to-year basis and contingent upon the appropriation and availability of funds.

#### REVIEW CONSIDERATIONS

Completed applications to the LRP are reviewed by the LRAC. The LRAC, which is composed of intramural and extramural scientific staff, reviews, ranks, and approves or disapproves applicants. LRAC approval, in part, is based on the appropriateness of the applicant's research assignment to AIDS research and the scientific merit of the research. In addition, the credentials provided in the application are reviewed and ranked to assess the applicant's potential to conduct qualified AIDS research.

#### AWARD CRITERIA

The award of funds for approved applications is contingent, in part, upon the availability of funds appropriated by the Congress of the United States for the NIH. In return for the repayment of educational loans, participants must agree (1) to be "primarily" engaged in qualified AIDS research, which is described above in the "Activities Constituting AIDS Research" criteria, as NIH employees for a minimum period of two years; (2) make payments to lenders on their own behalf for periods of Leave Without Pay (LWOP); (3) pay monetary damages as required in cases where the initial contract is breached; and (4) all other provisions agreed upon in the contracts. Substantial monetary penalties will be imposed for breach of contract.



## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Information regarding the LRP may be obtained by calling or writing the following:

Marc S. Horowitz, J.D.  
Director, NIH Loan Repayment Program for AIDS Research  
Office of AIDS Research  
National Institutes of Health  
Building 31, Room 5C12  
Bethesda, MD 20892  
Telephone: (800) 528-7689

## AUTHORITY AND REGULATIONS

The LRP is described in the Catalog of Federal Domestic Assistance No. 93.936. Awards are made under authorization of section 487A of the PHS Act (42 U.S.C. 288-1), as amended by section 634 of the Health Omnibus Programs Extension of 1988 (P.L. 100-607). This program is not subject to the provisions of Executive Order 12372, Intergovernmental Review of Federal Programs, and was granted clearance from the Office of Management and Budget (OMB) (0925-0361), under the requirements of the Paperwork Reduction Act of 1980, on June 15, 1990.

## DISCONTINUATION OF THE NCRR PROGRAM ANNOUNCEMENT: SMALL GRANTS FOR THE DEVELOPMENT OF NONMAMMALIAN MODELS

NIH GUIDE, Volume 21, Number 27, July 31, 1992

P.T. 34; K.W. 1004005, 0755020, 0780015

National Center for Research Resources

Beginning with the October 1, 1992, application receipt date, the National Center for Research Resources (NCRR) will no longer accept new and amended applications for the Biological Models and Materials Research (BMMR) Program Announcement for Small Grants for the Development of Nonmammalian Models as described in the NIH Guide for Grants and Contracts (Vol. 20, No. 24, June 21, 1991) under PA-91-68.

This decision was reached because program staff wish to examine the success of this announcement over the last year and determine if it will be useful to reissue another small grants program announcement for new nonmammalian model systems in the near future.

## INQUIRIES

Inquiries regarding this notice are to be addressed to:

Elaine Young, Ph.D.  
Biological Models and Materials Research Program  
National Center for Research Resources  
National Institutes of Health  
5333 Westbard Avenue, Room 8A07  
Bethesda, MD 20892  
Telephone: (301) 402-0630

## NOTICES OF AVAILABILITY (RFPs AND RFAs)

### SUPPORT SERVICES FOR THE NATIONAL ADVISORY BOARD AND RELATED OTHER SERVICES

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFP AVAILABLE: NIH-NIAMS-92-3

P.T. 01; K.W. 0755018

National Institute of Arthritis and Musculoskeletal and Skin Diseases

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) is seeking an organization to provide logistical, technical, analytical, and science writing assistance for the National Advisory Board for Arthritis and Musculoskeletal and Skin Diseases, two interagency committees, and the Office of the Director, NIAMS. Included in this project are activities related to the planning and coordination of the NIAMS programs. Assistance is required in the formulation of research plans; the conduct of scientific workshops, conferences, and task forces; the collection, analysis, and reporting of data; the preparation of periodic and special reports for the NIH Director, the Secretary, DHHS, the Congress, and the scientific community; and the development and preparation of health information for the practicing community and public. Specific services required include:

o Administrative, programmatic, technical, and analytic support for special initiatives including the development of the national plan for arthritis and musculoskeletal and skin diseases. These activities may be initiated by the working groups or task forces composed of members of the Advisory Board, interagency representatives, and the scientific community. The contract personnel will be required to interact and communicate with scientists and others associated with the NIAMS on university campuses and at other Federal and non-Federal organizations.



o Administrative, logistic, programmatic, technical, and analytical support for Advisory Board meetings and site visits, and support for scientific conferences and workshops of interest to the Advisory Board and its committees, the interagency committees, and the Office of the Director.

o Preparation of a variety of documents including scientific reports; background or issue papers; data analyses, such as prevalence and incidence data, and special reports; and health education materials that stem from meetings, subcommittee deliberations, workshops, and conferences. This will include writing, editing, design, production, and distribution.

This Request for Proposals (RFP) NIH-NIAMS-92-3, will be issued on or about July 20, 1992, with a proposed closing date of September 21, 1992. It is expected that this project will have a five year period of performance. To receive a copy of this RFP, supply this office with two self-addressed mailing labels and cite the RFP number referenced above. Requests must be in writing and addressed to:

Shirley A. Shores  
Contracts Management Branch  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 606  
Bethesda, MD 20892

This advertisement does not commit the Government to make an award.

#### TOXICITY OF LEAD IN CHILDREN TRIAL: CLINICAL CENTER

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFP AVAILABLE: NIH-ES-92-31

P.T. 34; K.W. 0755015, 1007009, 0740018

National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences seeks approximately three Clinical Centers for a clinical trial, the Toxicity of Lead in Children Trial. The objective of the trial is to test the use of the drug succimer in preventing lead-induced developmental delay. Children eligible for the trial will be about two years old and will be followed until they are at least four. The trial will be double blind to the extent possible. The target lead levels will be between about 20  $\mu\text{g/dl}$  to 45  $\mu\text{g/dl}$ . All children thought to be eligible will be treated for iron deficiency, be given vitamin and mineral supplementation, and have dust control measures instituted in their homes.

It is anticipated that there will be three Clinical Centers and one Coordinating Center (Request for Proposals NIH-ES-92-32). Clinical Centers will cooperate with the Coordinating Center and the other two Clinical Centers in developing, testing, and refining the overall program and in writing the final protocol, Manual of Operations, and training materials before recruitment commences. Each Clinical Center will be responsible for screening, recruitment, randomization, treatment, developmental testing, and follow-up of study subjects. Optimally, no more than three Clinical Centers will randomize to drug or placebo on the order of 1000 total children during a 1-year enrollment and treatment phase.

The Government estimates that an average of five professional FTEs, two technical FTEs, one clerical FTE, and one other FTE will be required on an annual basis per Clinical Center. The estimated period of performance is five years. Release date of the RFP will be on or about August 6, 1992 with proposals due November 4, 1992. All responsible sources may submit a proposal that will be considered by the agency.

Requests for the RFP must reference RFP NIH-ES-92-31 and must be forwarded to:

National Institute of Environmental Health Sciences  
Contracts and Procurement Management Branch  
ATTN: Thomas M. Hardee, Contracting Officer  
79 T.W. Alexander Drive, 4401 Building  
P.O. Box 12874  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7893  
FAX: (919) 541-2712

#### TOXICITY OF LEAD IN CHILDREN TRIAL: COORDINATING CENTER

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFP AVAILABLE: NIH-ES-92-32

P.T. 34; K.W. 0755015, 1007009, 0755018

National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences seeks a Coordinating Center for a clinical trial, the Toxicity of Lead in Children Trial. The objective of the trial is to test the use of the drug succimer in preventing lead-induced developmental delay. Children eligible for the trial will be about two years old and will be followed until they are at least four. The trial will be double blind to the extent possible. The target lead levels will be between about 20  $\mu\text{g/dl}$  to 45  $\mu\text{g/dl}$ . All children thought to be eligible will be treated for iron deficiency, be given vitamin and mineral supplementation, and have dust control measures instituted in their homes.

It is anticipated that there will be three Clinical Centers (Request for Proposals NIH-ES-92-31) and one Coordinating Center. The Coordinating Center will cooperate with the three Clinical Centers in developing, testing, and refining the overall program and in writing the final protocol, Manual of Operations, and training materials before recruitment commences. The Coordinating Center will plan randomization of study subjects. Optimally, no more than three Clinical Centers will randomize to drug or placebo on the order of 1000 total children during a 1-year enrollment and treatment phase.

The Government estimates that an average of five professional FTEs, two technical FTEs, one clerical FTE, and one other FTE will be required on an annual basis. The estimated period of performance is six years. Release of the RFP will be on or about August 6 with proposals due November 4, 1992. All responsible sources may submit a proposal that will be considered by the agency.

Requests for the RFP must reference RFP NIH-ES-92-32 and must be forwarded to:

National Institute of Environmental Health Sciences  
Contracts and Procurement Management Branch  
ATTN: Thomas M. Hardee, Contracting Officer  
79 T.W. Alexander Drive, 4401 Building  
P.O. Box 12874  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7893  
FAX: (919) 541-2712

CARDIOVASCULAR HEALTH STUDY: ECHOCARDIOGRAPHY READING CENTER

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFP AVAILABLE: NHLBI-HC-92-34

P.T. 34; K.W. 0715040, 0706030, 0755018, 0745020

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (NHLBI) requires a reading center to measure and interpret echocardiographic images performed on participants in the Cardiovascular Health Study (CHS), an epidemiological research study of the risk factors for the development and progression of coronary heart disease and stroke in the elderly in four U.S. communities. The Echocardiography Reading Center will assist in protocol development for the performance of echocardiographic examinations of study participants, train CHS Field Center staff at four sites, perform measurements and interpretations of 120 studies per week (5407 initial studies and 541 blind duplicates) in a standardized and reproducible manner, and participate in analysis and publication of data in collaboration with other study investigators and NHLBI staff. The period of performance is anticipated to be July 1, 1993 through May 30, 2000.

This is an announcement for a Request for Proposals (RFP). RFP NHLBI-HC-92-34 will be issued on or about July 24, 1992, and proposals will be due October 8, 1992. One award is anticipated to be made during July 1993. All responsible sources may submit a proposal that will be considered by the NHLBI. Send a written request with three self-addressed mailing labels and cite RFP NHLBI-HC-92-34. Telephone requests will not be accepted.

Requests for copies of the RFP are to be sent to:

Patricia A. Smith, Contracting Officer  
ECA Contracts Section  
Contracts Operations Branch, DEA  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3C16  
Bethesda, MD 20892

CARDIOVASCULAR HEALTH STUDY: ULTRASOUND READING CENTER

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFP AVAILABLE: NHLBI-HC-92-35

P.T. 34; K.W. 0715040, 0607024, 0706030, 0755018

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (NHLBI) requires a reading center to measure and interpret ultrasound images performed on participants in the Cardiovascular Health Study (CHS), an epidemiological research study of the risk factors for the development and progression of coronary heart disease and stroke in the elderly in four U.S. communities. The Ultrasound Reading Center will assist in protocol development for the performance of B-scan and doppler examinations of study participants, train CHS Field Center staff at four sites, perform measurements and interpretations of 112 studies per week (5,089 initial studies and 509 blind duplicates) in a standardized and reproducible manner, and participate in analysis and publication of data in collaboration with other study investigators and NHLBI staff. The period of performance is anticipated to be July 1, 1993 through May 30, 2000.

This is an announcement for a Request for Proposals (RFP). The RFP will be issued on or about July 24, 1992, and proposals are due October 7, 1992. One award is anticipated to be made during July 1993. All responsible sources may submit a proposal that will be considered by the NHLBI. Send a written request with three

self-addressed mailing labels and cite RFP NHLBI-HC-92-35. Telephone requests will not be accepted.

Requests for copies of the RFP are to be sent to:

Patricia A. Smith, Contracting Officer  
ECA Contracts Section  
Contracts Operations Branch, DEA  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3C16  
Bethesda, MD 20892

#### EPIDEMIOLOGY OF OVARIAN CANCER

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFA AVAILABLE: CA-92-20

P.T. 34; K.W. 0785055, 0715035, 0755030

National Cancer Institute

Letter of Intent Receipt Date: October 15, 1992

Application Receipt Date: November 12, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Cancer Etiology of the National Cancer Institute (NCI) invites grant applications for innovative interdisciplinary epidemiologic studies to better understand the etiology of ovarian cancer and the means of prevention.

The purpose of this RFA is to stimulate innovative interdisciplinary epidemiologic studies to better understand the etiology of ovarian cancer and the means of prevention.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Epidemiology of Ovarian Cancer, is related to the priority area of cancer. Potential applicants may obtain a copy of a "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, non-profit and for-profit institutions, public and private, such as colleges, universities, hospital, research laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from or involving minority institutions and individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will be supported through the NIH traditional research project grants (R01) and Interactive Research Project Grants (IRPG). For IRPGs, a minimum of three investigators with related research objectives may concurrently submit collaborative, cross-referenced individual research project grant applications that share a common focus. Applications may be from either a single institution or a consortium of institutions. Such applications will be reviewed independently for scientific merit and will be considered for funding both as independent awards and in the context of the overall proposed collaboration. Awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

The earliest anticipated date of award is July 1, 1993.

This RFA is a one-time solicitation. The total project period for applications submitted in response to the present RFA may not exceed five years. Competitive continuation applications will compete with all other unsolicited applications and be reviewed by standing Division of Research Grants study sections. If the NCI determines that there is a sufficient continuing program need, the NCI may announce a request for renewal applications.

#### FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for this initiative is \$2.0 million. The expected number of awards is five to eight. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the NCI, the award of grants pursuant to this RFA is contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

This initiative permits a range of epidemiologic and interdisciplinary investigations of ovarian cancer including, but not limited to:

### o Epidemiologic studies of

- the long-term effect of combination oral contraceptives, with special reference to age at initial use and age at cessation of use, on ovarian cancer risk by pathologic type;
- the relationship between hormone replacement therapy and ovarian cancer risk;
- the use of fertility-promoting drugs, ovarian stimulants, or in vitro fertilization in relation to ovarian cancer risk;
- the interrelationship of tubal ligation, hysterectomy, and hormone levels to ovarian cancer risk;
- the association of unilateral oophorectomy and age at oophorectomy with ovarian cancer risk;
- the influence of diet and physical activity and their interaction on ovarian cancer risk;
- the relationship of exposure to potential oocyte toxins, such as talc, galactose, caffeine, smoking, and other agents, to ovarian cancer risk among women who use and those who do not use oral contraceptives.

o Molecular epidemiology studies exploring differences in genetic predisposition to ovarian cancer due to variations in susceptibility genes, hormone metabolism, DNA repair activities, chromosome sensitivity to mutagens, or other factors.

o Molecular epidemiologic studies using existing registries of ovarian cancer families.

o Analytic studies of ovarian cancer to determine the impact of changes in exposure due to migration from low- to high-risk regions and/or to secular changes in lifestyle and environment.

o Studies of racial/ethnic differences in the histologic and cytologic parameters of ovarian cancer that may reflect differences in exposure or susceptibility.

o Population-based studies of the correlation of estrogen and progesterone receptor content of ovarian tumors with histologic type, grade, clinical prognosis, and exposure history.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

### LETTER OF INTENT

Prospective applicants are requested to submit, by October 15, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the names of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid conflict of interest in review. The letter of intent is to be sent to Dr. A.R. Patel at the address under INQUIRIES.

### APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91), available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7441. The format and instructions applicable to regular research grant applications must be followed. Applications must be received by November 12, 1992.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator must be included with the application.

IRPG applications may be submitted from a single institution or may include arrangements with one or more other institutions if appropriate. Each application will be considered on its own merit as an individual research project. Therefore, applicants for IRPGs MAY NOT concurrently submit R01 applications that represent significant duplication of the efforts described in the applicant's IRPG. In this regard, it should be noted that the NCI will consider funding meritorious individual IRPG applications if it is not possible to fund the IRPG package as a whole. (Interactive Research Project Grants for Cancer, PA-92-29, NIH Guide for Grants and Contracts, Vol. 21, No. 1, January 10, 1992). Concurrent submission of program project applications are prohibited.



## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Preliminary evaluation for responsiveness to the RFA is an NCI program staff function. If an application is judged to be nonresponsive, the applicant will be contacted and given an opportunity to have it considered along with other unsolicited grant applications received by NIH.

Applications responsive to this solicitation will be reviewed by an appropriate review group convened by the Division of Extramural Activities, NCI. The initial review will be for scientific merit. The second level of review by the National Cancer Advisory Board considers the special needs of the NCI and the priorities of the National Cancer Program.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications.

- o scientific, technical, or medical significance and originality of proposed research;
- o appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;
- o qualifications and research experience of the Principal Investigator and staff, particularly but not exclusively in the area of the proposed research;
- o availability of resources necessary to perform the research.

The review group will critically examine the submitted budget and will recommend an appropriate budget and period of support for each scored application.

## AWARD CRITERIA

In addition to technical merit, reasonableness of the budget in comparison with other applications will be taken into consideration in making an award.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. A.R. Patel  
Extramural Programs Branch  
Epidemiology and Biostatistics Program  
Division of Cancer Etiology  
National Cancer Institute  
6130 Executive Boulevard  
Executive Plaza North, Suite 535  
Rockville, MD 20892  
Telephone: (301) 496-9600

Direct inquiries regarding fiscal matters to:

Ms. Jean M. Cahill  
Supervisory Grants Management Specialist  
National Cancer Institute  
6120 Executive Boulevard  
Executive Plaza South, Suite 243  
Rockville, MD 20892  
Telephone: (301) 496-7800, ext. 47

## AUTHORITY AND REGULATIONS

This cancer cause and prevention research program is described in the Catalog of Federal Domestic Assistance No. 93.393. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health System Agency review.

## BIOTECHNOLOGY TRANSFER TO EPIDEMIOLOGIC STUDIES IN CANCER

NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFA AVAILABLE: CA/ES-92-23

P.T. 34; K.W. 0715035, 0760003, 0785055, 0411005

National Cancer Institute  
National Institute of Environmental Health Sciences

Letter of Intent Receipt Date: October 22, 1992  
Application Receipt Date: November 19, 1992

THE REQUEST FOR APPLICATION (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

#### PURPOSE

The Extramural Programs Branch, Division of Cancer Etiology, National Cancer Institute (NCI), and the Scientific Programs Branch, Division of Extramural Research and Training, National Institute of Environmental Health Sciences (NIEHS), invite investigator-initiated research grant applications to further the effective use of biomarkers of exposure or susceptibility in future epidemiologic studies of cancer etiology.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Biotechnology Transfer to Epidemiologic Studies in Cancer, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign non-profit and for-profit institutions, public and private, such as colleges, universities, hospitals, research laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This program will be supported by traditional research project (R01) grants and Interactive Research Project grants (IRPG). Awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

The earliest anticipated date of award is July 1, 1993.

This RFA is a one-time solicitation. The total project period for applications submitted in response to the present RFA may not exceed three years. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Competitive continuation applications will compete with all other unsolicited applications and be reviewed by standing Division of Research Grants study sections. If the NCI and NIEHS determine that there is a sufficient continuing program need, a request for renewal applications may be announced.

#### FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for this initiative is \$1.5 million. The expected number of awards is five to seven. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI and the NIEHS, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

#### SPECIAL REQUIREMENTS

Successful grant awardees under this RFA are strongly encouraged to participate in an annual program meeting of one or two days' duration in Bethesda, Maryland, during the first and third years and in Research Triangle Park, North Carolina during the second year. Program directors from the NCI and the NIEHS will coordinate the meeting that will review and assess overall progress and provide the opportunity for investigators to exchange information and discuss methodological issues. The respondents must request sufficient funds within the budget to accommodate expenses for one to two participants at these meetings. The application should include a statement indicating a willingness to comply with this requirement.

#### RESEARCH OBJECTIVES

##### Background

A large proportion of human cancers are thought to be attributable to environmental factors, some of which may interact with host susceptibility states. The problem of identifying the effects of specific risk factors and evaluating their relative importance is a challenging one. Multiple exposures to a variety of agents over extended periods are the rule rather than the exception, and many populations are exposed to low levels of carcinogens. A wide range of susceptibility mechanisms may be involved in processes of carcinogenesis, and the long latency period of many cancers may make cause-effect relationships elusive.

Traditional methods in epidemiology have estimated exposure to carcinogens on the basis of surrogate measures. These have included, for instance, questionnaire data on lifestyle factors such as diet and smoking, record of job titles or past employment in a particular industry, or interview information on use of medications. Discovery of the association between smoking and lung cancer is a classical example, demonstrating the merit of these techniques. In etiological studies, the addition of measured parameters in the form of biological markers (biomarkers) can strengthen epidemiologic findings, especially where there may be a weak causal effect, differences in exposure level, complex mixtures of agents, or interactions of risk factors. Appropriate biomarkers can reduce misclassification of exposures, increase accuracy, and enhance study power to resolve exposure-cancer relationships.

Exciting opportunities have emerged from the recent revolution in molecular biology and genetics. Laboratory advances offer unprecedented capabilities to measure carcinogenic factors at the cellular or molecular level and to detect their interaction with cellular constituents. A variety of biomarkers (e.g., biochemical, molecular, genetic, immunologic) show significant promise of improving exposure assessments (e.g., hemoglobin or DNA adducts), identifying inherited and acquired host susceptibility (e.g., p53 gene mutations), and detecting cellular and subcellular events representing predisposing disease states, intermediate outcomes, and early stages of cancer (e.g., sister chromatid exchanges). To date, most of the evidence about biomarkers has been derived from experimental systems, with only limited testing in human subjects in well-controlled field studies. Pilot studies in small populations of humans have demonstrated the utility of certain biomarkers: cellular assays indicating pathobiological responses to carcinogens (e.g., cytogenetic changes) and techniques that assess inherited or acquired host susceptibility factors (e.g., metabolic polymorphic phenotyping). However, a wide range of interindividual variability and methodological issues remain to be resolved before these procedures can be applied to large-scale epidemiologic investigations.

#### Other

The goal of this initiative is to stimulate investigations designed to validate and apply biomarkers of exposure or susceptibility in epidemiologic research in cancer etiology. For biomarkers demonstrated to have utility, assessment of the extent of intra- and inter-individual variability is important. Validation procedures should consider determinations of range of normal values, as well as sensitivity, specificity, and predictive value. The influence of biological variables such as age, sex, race, ethnicity, nutritional status, preexisting disease, and lifestyle should be appropriately addressed.

Inter-institutional collaborations between laboratory scientists from several disciplines and epidemiologists are encouraged to promote integrated planning of study protocols and experimental methods as well as the conduct of research. Extension of an ongoing epidemiologic study by the addition of a laboratory component can be proposed. Laboratory investigations will be acceptable if human subjects or specimens are being tested. Whenever possible, research design should utilize shared laboratory and specimen resources. Ease of study conduct and expense, as well as collection, storage, and transport problems should be considered. Projects will be evaluated on their potential for enhancing the understanding of cancer etiology and strategies for prevention. We particularly encourage studies with relevance to breast, ovarian, prostate, and cervical cancers.

The initiative permits a range of investigations in molecular epidemiology relevant to cancer etiology, including, but not limited to:

- o Demonstration of the feasibility of developed biomarkers for epidemiologic research (e.g., heterocyclic amine food mutagens, benzene-DNA adducts, thymine glycol, mutation of the hypoxanthine guanine phosphoribosyl transferase (HGPRT) gene);
- o Validation of biomarkers in exposed and unexposed population subgroups (e.g., ethnic and minority populations, family units, occupational cohorts, patients taking chemotherapeutic agents or other medicinal compounds);
- o Determination of levels of agreement of mutually confirmatory methods of analyses for measuring the same biomarker (e.g., DNA adducts by physico-chemical, immunoassay, and postlabelling methods) with consideration of inter- and intra-laboratory variability;
- o Comparison of biomarkers or combinations of biomarkers in different sources of specimens such as human cells, tissues, organs, and body fluids;
- o Determination of specific sampling conditions (e.g., timing, seasonality, repetitive or serial testing) in a chronobiologic fashion including host/environmental factors with/without interactions (e.g., dietary, viral, hormonal) that may influence validity, reliability, and reproducibility;
- o Establishment of background or reference levels in normal or unexposed populations (e.g., cytochrome P450 isoenzymes, glucuronyltransferase, covalent RNA or protein adducts, arylamine-macromolecular adducts).

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are requested to submit, by October 22, 1992, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NCI and NIEHS staff to estimate the potential review workload. The letter of intent is to be sent to Dr. Kumiko Iwamoto at the address under INQUIRIES.

## APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91), available at most institutional business offices and from the Office of Grants inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7441. The format and instructions applicable to research grant applications must be followed. Applications must be received by November 19, 1992.

## REVIEW CONSIDERATIONS

Each application submitted in response to the RFA will be given dual institute assignment to the NCI and the NIEHS. The primary assignment will be determined later by mutual agreement of the Program Directors from the supporting programs. Applications judged to be competitive will be reviewed by an appropriate review panel of the Division of Extramural Activities, NCI. Second level review will be by the National Cancer Advisory Board or the National Advisory Environmental Health Sciences Council. All applications will be reviewed in competition with each other.

The factors that will be considered in evaluating grant applications that are responsive to this RFA will include: scientific, technical, or medical significance and originality of proposed research; appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research; qualifications and research experience of the Principal Investigator and staff, particularly but not exclusively in the area of the proposed research; availability of resources necessary to perform the research; and appropriateness of the proposed budget and duration in relation to the proposed research.

## INQUIRIES

Written and telephone inquiries concerning the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Kumiko Iwamoto  
Extramural Programs Branch  
Epidemiology and Biostatistics Program  
Division of Cancer Etiology  
National Cancer Institute  
Executive Plaza North, Suite 535  
Rockville, MD 20892  
Telephone: (301) 496-9600

or

Dr. William A. Suk  
Scientific Programs Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
Research Triangle Park, NC 27709  
Telephone: (919) 541-0797

Direct inquiries regarding fiscal matters to:

Ms. Jean M. Cahill  
Supervisory Grants Management Specialist  
National Cancer Institute  
6120 Executive Boulevard  
Executive Plaza South, Suite 216  
Rockville, MD 20892  
Telephone: (301) 496-7800, ext. 47

or

Mr. David L. Mineo  
Grants Management Officer  
Grants Management Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-1373

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.393, Cancer Cause and Prevention Research. Awards are made under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.



NIH GUIDE, Volume 21, Number 27, July 31, 1992

RFA AVAILABLE: CA-92-21

P.T. 34; K.W. 0715035, 0785055, 1010013

National Cancer Institute

Letter of Intent Receipt Date: September 30, 1992

Application Receipt Date: November 12, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Cancer Etiology of the National Cancer Institute (NCI) announces the availability of an RFA to stimulate interest in small projects for the transfer of theoretical biostatistical methodologies to application in cancer epidemiologic studies.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Transfer of New Biostatistic Methods to Cancer Epidemiology, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority and women investigators are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed three years. The earliest anticipated date of award will be July 1, 1993.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary NIH peer review procedures.

#### FUNDS AVAILABLE

Approximately \$500,000 in total costs will be committed for the first year to fund applications submitted in response to this RFA. The intent is to fund 5 to 10 small research awards.

This level of support is dependent on the receipt of sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI awards pursuant to this RFA are also contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The purpose of this RFA is to stimulate collaborations and interactions among theoretical and applied biostatisticians, cancer epidemiologists, computer scientists, and programmers and to promote the introduction of appropriate theoretical methods to epidemiologic projects in cancer research. In many instances these grants will be small addenda to approved biostatistical and epidemiological R01 grants. This initiative proposes to link peer-approved activities to provide a mechanism for facilitating the transfer of new biostatistical methodologies to applied biostatisticians and epidemiologists. The goal is to ensure the validation and integration of promising new statistical and computing techniques into epidemiologic studies. Projects funded by this initiative will lead to substantial cost savings by developing computer programs and analytical techniques that can be shared by numerous projects. It is not the intent of this RFA to fund the development of commercial programs or packages.

This RFA encourages the development of 5 to 10 small projects that will each provide enough support for one key researcher with expertise in the application of theory to real-life problems in cancer research, with appropriate collaborations. Subjects of interest include, but are not limited to:

- o Cox regression model
- o Logistic regression model, ordered logistic regression
- o Polychotomous regression model
- o Sequential trials; group sequential trials
- o Multiple endpoints
- o Surrogate endpoints
- o Time-dependent covariates

- o Censored data; left and right truncation
- o Meta-analysis
- o Data augmentation methods (Gibbs, bootstrap, and jackknife methods)
- o Martingales: counting processes in survival analysis
- o Frailties
- o Repeated measures
- o Determination of maximum tolerated dose
- o Surrogate markers of exposure

#### LETTER OF INTENT

Prospective applicants are asked to submit, by September 30, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to Dr. Marthana C. Hjortland at the address under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91), available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7441. The format and instructions applicable to research grant applications must be followed.

Applications must be received by November 12, 1992.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Preliminary evaluation for responsiveness to the RFA is an NCI program staff function. If an application is judged to be nonresponsive, the applicant will be contacted and given an opportunity to have it considered along with other unsolicited grant applications.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications. Those factors considered in the review include:

- o extent to which application addresses research objectives of RFA;
- o overall scientific merit;
- o quality of collaborations to facilitate transfer;
- o qualifications, research experience, and time commitment of investigators;
- o adequacy of facilities and resources;
- o cost effectiveness of the application.

The review group will critically examine the submitted budget and will recommend an appropriate budget and period of support for each scored application.

#### AWARD CRITERIA

The earliest anticipated date of award is July 1, 1993.

In addition to technical merit, the overall applicability to analysis of data from cancer research studies will be taken into consideration in making an award.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Marthana C. Hjortland  
 Extramural Programs Branch  
 Epidemiology and Biostatistics Program  
 Division of Cancer Etiology  
 National Cancer Institute  
 6130 Executive Boulevard  
 Executive Plaza North, Suite 535  
 Rockville, MD 20892  
 Telephone: (301) 496-9600

Direct inquiries regarding fiscal matters to:

Ms. Jean M. Cahill  
Supervisory Grants Management Specialist  
National Cancer Institute  
6120 Executive Boulevard  
Executive Plaza South, Suite 243  
Rockville, MD 20892  
Telephone: (301) 496-7800, ext. 47

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.393. Awards are made under authorization of the Public Health Service Act, Title IV, and Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### NEURO-AIDS: HIV-I INFECTION AND THE NERVOUS SYSTEM

NIH GUIDE, Volume 21, Number 27, July 31, 1992

PA NUMBER: PA-92-95

P.T. 34; K.W. 0715008, 0705055, 1002030

National Institute of Neurological Disorders and Stroke  
National Institute of Mental Health

#### PURPOSE

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Mental Health (NIMH), components of the National Institutes of Health (NIH), invite research grant applications through this Program Announcement (PA) for support of research on neurological aspects of human immunodeficiency virus (HIV) infection (neuro-AIDS) in adults and children. It is well recognized that HIV-I infection, directly and/or indirectly, causes central and peripheral nervous system abnormalities that later may be compounded by opportunistic infections and malignancies. Applications are solicited covering a broad range of activities in the neurological sciences from basic research to diagnosis and management of neurological complications including therapeutic investigations of HIV-related neurological disease in adults and children. Research applications supporting the establishment or enlargement of collaborative and consultative neurologic units coordinated with AIDS Clinical Treatment Units (ACTUs) of the AIDS Clinical Treatment Group (ACTG), Women and Infants Transmission Study (WITS), and Multicenter AIDS Cohort Study (MACS) supported by the National Institute of Allergy and Infectious Diseases (NIAID) are especially solicited but are not required.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Neuro-AIDS: HIV-I Infection and the Nervous System, is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic institutions, for-profit and non-profit organizations, public or private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Foreign institutions are only eligible to apply for research project grants (R01). Applications from minority institutions, minority individuals, and women are particularly encouraged.

#### MECHANISMS OF SUPPORT

Research support may be requested through application for an individual investigator originated Research Project Grant (R01). Applications from new investigators who have not received previous PHS research grant support may apply for a First Independent Research Support and Transition (FIRST) Award (R29). To apply for the support of a more broadly based multidisciplinary research program, the Research Program Project (P01) mechanism is suggested.

#### RESEARCH OBJECTIVES

Neurological abnormalities and associated psychomotor and neurodevelopmental problems may be the first presenting symptoms of AIDS. Many advanced AIDS patients exhibit neurological dysfunction, and as many as 90 percent of the cases may demonstrate neuropathological changes at autopsy. It appears that the AIDS virus enters and affects the nervous system by way of macrophage infection and release of neurotoxic cytokines.

In primary neuro-AIDS, involvement of every level of the central and peripheral nervous system (PNS) has been reported: dementia, meningitis, encephalitis, encephalopathy, myelopathy, peripheral neuropathy, and



polymyositis. Myopathies, neuropathies, and other neurological side effects of current treatment are also known. Management and treatment of neurological complications of opportunistic infection and HIV related malignancies remains a significant challenge.

This PA is an NINDS and NIMH call for increasing the effort on research studies of neuro-AIDS in adults and children. Increasing recognition of neurological aspects and complications of AIDS indicates that recruitment and greater involvement of neuroscientists in this disease is desirable. This PA is intended to motivate individual scientists, inter-disciplinary research teams, and collaborative alliances to apply for research support to establish financially autonomous, but scientifically integrated, neuro-AIDS research nuclei particularly in partnership with ACTUs, MACS, and WITS.

Examples of research objectives appropriate for an application in response to this PA include:

- o Studies of HIV-1 infection of the CNS and subsequent neuro-AIDS complications in adults and children;
- o Studies of AIDS-associated disorders of the PNS and resulting dysfunctions and abnormalities;
- o Studies of the neurological complications of AIDS and its treatment and of opportunistic infections and malignancies;
- o Studies of prevention, control, and treatment of opportunistic infections of the nervous system, such as progressive multifocal leukoencephalopathy cytomegalovirus toxoplasmosis, and fungal infections;
- o Neuro-imaging studies of the manifestations of neuro-AIDS including positron emission tomography magnetic resonance imaging, magnetic resonance spectroscopy;
- o Epidemiological studies of neuro-AIDS.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaska Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned to the applicant without review.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted for an accelerated review cycle on any of the three AIDS application receipt dates: September 1, January 2, and May



1. Only applications submitted for the September and January deadlines would qualify for Fiscal Year 1993 funds. The NINDS Application Guidelines (rev. 4/92) for Program Project (P01) Grants are available upon request from the Program Administrator identified below (see INQUIRIES).

Application kits are available at most business and grants and contracts offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

On the first (face) page, item 2a of the application, the word "yes" must be checked and the title and number of the announcement typed in the space provided: "Neuro-AIDS: HIV-I Infection and the Nervous System, PA-92-95."

The original and five copies of the application must be sent or delivered to:

Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

The Division of Research Grants, NIH, serves as a central point for receipt of applications.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources, and/or ACTUs, MACS, and WITS funded by the NIAID may wish to identify the GCRC and/or ACTUs, MACS, and WITS as a resource for conducting the proposed research. In such a case, a letter of collaboration from the GCRC, ATCU, MACS, and WITS Program Director or Principal Investigator must be included with the application.

#### REVIEW CONSIDERATIONS

Applications received under this PA will be assigned to the Initial Review Group (IRG) in accordance with established PHS referral guidelines. The IRGs, which are composed primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit. Following IRG review, the applications will receive a second-level review by one or more appropriate advisory councils.

#### AWARD CRITERIA

The standard review criteria will be used to assess the scientific merit of applications.

Applications will compete for available funds with all other applications. The following will be considered when making funding decisions:

- o Quality of the proposed projects as determined by peer review;
- o Availability of funds;
- o Program balance among research areas.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. A. P. Kerza-Kwiatkowski  
Program Administrator  
Division of Demyelinating, Atrophic, and Dementing Disorders  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 804  
Bethesda, MD 20892  
Telephone: (301) 496-1431  
FAX: (301) 402-2060

or

Dr. Walter L. Goldschmidts  
Office of AIDS Programs  
National Institute of Mental Health  
Parklawn Building, Room 15-99  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-7281  
FAX: (301) 443-9719

Direct inquiries regarding fiscal matters to:

Ms. Laura Williams  
Grants Management Specialist  
Grants Management Branch, Division of Extramural Activities  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-9231  
FAX: (301) 402-0219



#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.853 and 93.242. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 28  
August 7, 1992

RICHARD W HURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES OF AVAILABILITY (RFPs AND RFAs)

IN VIVO TESTING

NIH GUIDE, Volume 21, Number 28, August 7, 1992

RFP AVAILABLE: NCI-CM-37821-12

P.T. 34; K.W. 0755060, 0780015

National Cancer Institute

Request for Proposals (RFP) Nos. NCI-CM-37821-12 (formerly NCI-CM-37821-28) and NCI-CM-37830-12 will be issued upon written request to Joyce Crooke, Contract Specialist, on or about August 7, 1992. Proposals will be due on or about September 28, 1992.

A major objective of the Developmental Therapeutics Program (DTP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI), is the testing for and evaluation of activity of compounds in in vitro cell lines and in vivo tumor systems. DTP is soliciting organizations having the necessary experience, scientific and technical personnel, and facilities to conduct in vivo testing of compounds that have demonstrated in vitro activity against a battery of human tumor cell lines. Secondary in vivo testing is essential in order to confirm activity of a compound and further define its specificity. The studies to be performed may require any or all of the following: direct on-site support at the Contractor's facility for in vitro expansion of cell lines and initial in vivo assays utilizing rapid and sensitive procedures; detailed follow-up in vivo studies; investigation into the effect of formulation, treatment schedules, route of drug administration, and site of tumor implantation on drug activity. The Contractor will be required to receive, maintain, and experimentally use regular and/or athymic nude mice; propagate and maintain tumor stock in vivo; prepare and administer test materials to tumor-bearing and nontumor-bearing animals; monitor the quality of all tumor lines and mice; determine test material activity; and report the results. The Government will designate and supply the agents to be tested. The Contractor will be expected to provide all equipment and animal facilities needed to conduct this type of work. The following Mandatory Qualification Criteria will apply: (1) the Contractor may not be a pharmaceutical or chemical firm since compounds of a commercially confidential nature (discreet) may be evaluated; (2) since structural formulae and other information on discreet compounds may be included, Contractors must be willing to sign a confidentiality of information statement.

RFP No. NCI-CM-37821-12, In Vivo Testing, is an open competition. RFP No. NCI-CM-37830-12, In Vivo Testing, is a 100 percent Set-Aside for Small Business. The Standard Industrial Code (SIC) is 8731. Offerors who



qualify as a small business are encouraged to submit proposals under both RFPs. It is anticipated that a total of two incrementally-funded, cost-reimbursement completion contracts will be awarded between these RFPs with the contract period beginning on or about June 1, 1993. The contract period will be five years.

#### INQUIRIES

RFP requests are to be addressed to:

Joyce Crooke  
Contract Specialist  
National Cancer Institute  
Executive Plaza South, Room 603  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-8628

No collect calls will be accepted.

#### ANIMAL MODELS OF HUMAN PAPILLOMAVIRUS INFECTIONS FOR EVALUATION OF EXPERIMENTAL THERAPIES

NIH GUIDE, Volume 21, Number 28, August 7, 1992

RFP: NIH-NIAID-DMID-93-05

P.T. 34; K.W. 1002045, 0755020, 0765033

National Institute of Allergy and Infectious Diseases

The Antiviral Research Branch of the Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, is seeking investigators to employ appropriate animal model systems of human papillomaviral infections to evaluate the efficacy of experimental therapies and provide basic information on the natural history and pathogenesis of papillomavirus infections.

Current treatment for papillomavirus infection is limited to topical therapies which destroy tissue, are limited to visible lesions, and are associated with unacceptably high recurrence rates. Consequently, there is a clear need to identify effective systemic chemotherapeutic agents. The availability of animal model systems mimicking human papillomavirus infection makes it feasible to continue a program to identify therapeutic agents for these infections.

The primary objective of the Animal Models Program of the Antiviral Research Branch is to evaluate experimental therapies for potential clinical efficacy and toxicity in animal models of clinically important human viral infections.

In addition, the animal models are used to study disease pathogenesis and host response to infection. In the future, when appropriate, these models will also be used for a limited amount of vaccine evaluation and pharmacokinetic studies. Animal models that are predictive of human response to a therapeutic intervention are invaluable for the identification of experimental therapies with the best clinical potential. They are also important for evaluation of dosing regimens, combination drug therapies and delivery strategies. The animal models program has made many significant contributions to the development of new therapies. This recompetition is planned to assure the continuation of this vital resource for the development of antiviral therapies. This program currently includes models of the following infections: influenza, parainfluenza, respiratory syncytial virus, measles, neonatal herpes, herpes encephalitis, genital herpes, varicella zoster virus, cytomegalovirus, and papillomaviruses.

The emphasis for this solicitation will be to support animal models that: (a) share significant features of pathology and natural history with human papillomavirus infections, (b) utilize either a human virus or an animal virus with considerable homology to the human virus, and (c) have been, or can be expected to be, predictive for human efficacy. As in the past, basic studies on model development, disease pathogenesis, and natural history will be encouraged as an adjunct to the primary focus on therapeutic evaluation. Occasionally, when appropriate, these models will also be utilized for vaccine evaluation and for pharmacokinetic analysis of a compound.

Any contract awarded will be subject to the Department of Health and Human Services regulations regarding the animal subjects in research. This announcement is a new solicitation. The issuance of the RFP will be on or about August 4, 1992 and proposals will be due at close of business on September 21, 1992. It is expected that two contracts with a five-year period of performance will be awarded as a result of this solicitation.

The request for the RFP should be addressed to:

Mr. Carl Henn  
Contracting Officer  
Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C07  
6003 Executive Boulevard  
Bethesda, MD 20892

Please provide this office with two self-addressed mailing labels.

This advertisement does not commit the Government to award a contract.

**RESEARCH ON TREATMENT EFFECTIVENESS FOR LEARNING DISABLED (LD) CHILDREN**

**NIH GUIDE**, Volume 21, Number 28, August 7, 1992

RFA AVAILABLE: HD-93-09

P.T. 34; AA; K.W. 0507005, 0410001

National Institute of Child Health and Human Development

Application Receipt Date: January 7, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

**PURPOSE**

The Human Learning and Behavior Branch (HLB) of the Center for Research for Mothers and Children (CRMC) of the National Institute of Child Health and Human Development (NICHD) invites research grant applications to develop new knowledge in the area of treatment effectiveness for learning disabled children, between the ages of six and twelve, who display primary deficits in oral and written language abilities including disabilities in listening, speaking, reading, and written language skills. The research emphasis must be placed on the identification, development, and implementation of treatment/intervention conditions that have effects on specific deficits in component oral language abilities (e.g., phonology, semantics, syntax), written language abilities (e.g., word attack skills, word recognition skills, reading comprehension, spelling behavior, written expression skills), and the relationships between them (e.g., compound disabilities in phonology, word attack skills, spelling, and written expression). However, children with comorbid deficits in attention, mathematics, behavioral and social competencies should also be studied in the process.

The goal of this RFA is to encourage treatment/intervention research on children with learning disabilities who are well-defined in terms of age, gender, ethnicity, socio-economic status, primary learning disability, comorbid disabilities (e.g., ADD; mathematics disability), severity of disability(ies), intensity and duration of previous and current interventions, familial and/or genetic findings, physical/neurological findings, intellectual status, cognitive-linguistic status, neurophysiological/neuropsychological status, educational status, and social/behavioral competencies.

**HEALTHY PEOPLE 2000**

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priorities. Of the 3000 such objectives, 170 address the public health needs of children and adolescents. This RFA, Research on Treatment Effectiveness for Learning Disabled (LD) Children, specifically addresses the priorities that are related to learning problems and psychosocial interventions in children. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-474-0, or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202/783-3238).

**ELIGIBILITY REQUIREMENTS**

Applications may be submitted by domestic public and private, non-profit and for-profit organizations such as universities, colleges, hospitals, schools, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply.

## MECHANISM OF SUPPORT

The support mechanism for this RFA is the Individual Research Grant (R01). Policies that govern are those of the grant-in-aid award programs covered by the PHS. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed five years.

## FUNDS AVAILABLE

The NICHD has set aside \$600,000 for direct costs for the first year of support. It is anticipated that two awards will be made. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the NICHD, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

A critical public health task confronting the field of learning disabilities is to understand and define the treatment/intervention variables and factors that have to be considered when addressing the oral and written language needs of LD children. There exists an immediate and compelling need to develop intervention protocols that increase the probability that individuals with well-defined LD will acquire proficient reading and written language skills as well as the skills that are related to these developmental learning processes. For a fuller elaboration of the possible research questions to be addressed, applicants may contact the program official identified under INQUIRIES below and request a copy of the RFA.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

The research subjects will be boys and girls between the ages of six and twelve. Investigators are encouraged to study male and female children varying in their racial and socio-economic background.

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## APPLICATION PROCEDURES

Applications are to be submitted on PHS form 398 (rev. 9/91). This application form is available in the business or grants and contracts office at most academic and research institutions and from the Office of Grants Inquiries, Division of Research Grants, NIH, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The receipt deadline for applications prepared in response to this RFA is January 7, 1993. Late applications will not be accepted.

## REVIEW CONSIDERATIONS

Applications will be reviewed by staff of the NICHD for responsiveness to the RFA. Applications deemed non-responsive will be returned to the applicant. In the event that an application is returned, the applicant has the option to resubmit the application to the Division of Research Grants as an unsolicited application during one of the three yearly review cycles (February 1, June 1, October 1). If the application submitted in response to this RFA is substantially similar to a grant application already submitted to the NIH for review, but has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application cannot be submitted in response to this RFA that is essentially identical to one that has already been reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

Responsive applications may be evaluated by preliminary triage in a peer review group to determine their scientific merit relative to other applications received in connection with this RFA. Applications judged to be non-competitive will not be considered further. The Principal Investigator and his/her institutional business official will be notified in such instances. Those applications judged to be competitive will be further evaluated for technical and scientific merit by a peer review panel convened for this purpose by the Division of Scientific Review, NICHD.

Review criteria will be those customarily used by the NIH to evaluate investigator-initiated R01 applications.

## INQUIRIES

Direct inquiries regarding programmatic information and requests for the RFA to:

G. Reid Lyon, Ph.D.  
Human Learning and Behavior Branch  
Center for Research for Mothers and Children  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-6591

Direct fiscal and administrative inquiries regarding this announcement to:

E. Douglas Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-1303

## AUTHORITY AND REGULATION

This program is described in the Catalog of Federal Domestic Assistance No. 93.865, Research for Mothers and Children. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42, USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. Awards are also made under authorization of PHS Act, Title V, Part B. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health System Agency review.

## BIOLOGY AND IMMUNOLOGY OF BREAST CANCER: AN INTERDISCIPLINARY APPROACH

NIH GUIDE, Volume 21, Number 28, August 7, 1992

RFA AVAILABLE: CA-92-24

P.T. 34; K.W. 0715035, 0710070, 0710030

National Cancer Institute

Letter of Intent Receipt Date: November 3, 1992  
Application Receipt Date: December 1, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS SHOULD OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The intent of this initiative is to encourage interdisciplinary approaches to research on the basic biology and immunobiology of breast cancer. In a recent workshop, a number of areas were identified that would benefit greatly from additional basic research carried out in a multidisciplinary context. These areas include immunology, molecular genetics, endocrinology, and cell biology of breast cancer development. The goal of this RFA is to encourage interactive grant applications that propose research with an interdisciplinary approach and that address unanswered questions in the field of breast cancer.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Biology and Immunology of Breast Cancer: An Interdisciplinary Approach, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).



## ELIGIBILITY REQUIREMENTS

Research grant applications from interactive groups may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Interactive Research Project Grant (IRPG) mechanism. Information about this mechanism of support is available in NCI program announcement PA-92-29. Each IRPG must contain at least three individual R01 applications, and address a minimum of two of the major areas of research interest listed in the Research Objective section of this RFA. Broader diversity of scientific areas is preferred and although not a requirement, applicants are encouraged to include one or more projects in immunology. One Principal Investigator out of the group must be identified as the "Program Coordinator," and must be cited in all applications on page 2 of form PHS 398. Applicants must describe how their integrated approach will provide a more comprehensive understanding of important problems in breast cancer basic research. The total project period for applications submitted in response to the present RFA may not exceed four years.

This RFA is a one-time solicitation. Generally, future unsolicited competing renewal applications as IRPGs or individual R01s will compete with all investigator-initiated R01 applications and be reviewed according to the customary peer review procedures by the Division of Research Grants (DRG).

## FUNDS AVAILABLE

Approximately \$1,500,000 in total costs per year for four years will be committed to fund applications that are submitted in response to this RFA. It is anticipated that at least two IRPG awards will be made, comprising a total of six to eight individual R01 grant awards. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. The earliest start date for the initial award will be July 1, 1993. Although this program is provided for in the financial plans of the NCI, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

The Division of Cancer Biology, Diagnosis, and Centers would like to support basic research in, but not restricted to, the following areas:

- o Immunobiology - Studies of both positive and negative effects of immune responses on breast cancer development and progression, molecular identification of relevant breast cancer antigens, and the development of effective strategies for immunologically-based prevention or treatment of breast cancer.
- o Cell Biology - Studies of the organization and differentiation of breast epithelial cells during normal development and progression to malignancy, including studies of interactions between normal and malignant epithelial cells and the surrounding tissue/stroma.
- o Molecular Genetics - Studies of the contribution of changes in the structure or regulation of oncogenes, tumor suppressor genes, and other important cellular genes to the development and biologic behavior of breast cancer.
- o Endocrinology (Hormones/Growth Factors) - Studies of the roles of soluble factors and their receptors in breast cancer development and the response to therapy. These may include, but are not limited to, steroid and nonsteroid factors such as estrogen, progesterone, insulin-like growth factor, prolactin, TGF-ALPHA and TGF-BETA.

The overall goal of this basic research in biology and immunology is to translate findings into practical clinical applications for early tumor detection and diagnosis, treatment of established tumors, and ultimately, for prevention intervention in high-risk women. However, these clinical and prevention applications are outside the scope of this RFA.

## SPECIAL REQUIREMENTS

Applicants must state clearly how they plan to collaborate. Applicants who already have ongoing collaborations must indicate how their response to this RFA will augment their current collaboration. Because the ultimate goal is to arrive at conclusions relevant to human breast cancer, projects that limit the entire studies to long-established tumor cell lines or animal models must justify the choice of the systems.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

### LETTER OF INTENT

The designated "Program Coordinator" of each prospective applicant group is asked to submit, by November 3, 1992, a letter of intent that includes descriptive titles of each individual investigator-initiated proposed research project, the names, institutions, addresses, and telephone numbers of the Principal Investigators, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Grace L.C. Shen  
Cancer Immunology Branch  
Division of Cancer Biology, Diagnosis, and Centers  
National Cancer Institute  
Executive Plaza South, Room 634  
6120 Executive Boulevard  
Rockville, MD 20892-9904  
Telephone: (301) 496-7815  
FAX: (301) 402-1037

### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892-9912, telephone 301/496-7441.

Details of the application procedures are available in the RFA.

### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete or non-responsive applications will be returned to the applicant without further consideration.

Only applications judged to be both responsive and competitive by NCI program staff will be further evaluated by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review will be by the National Cancer Advisory Board.

### INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Dr. Grace L.C. Shen  
Cancer Immunology Branch  
Division of Cancer Biology, Diagnosis, and Centers  
National Cancer Institute  
Executive Plaza South, Room 634  
6120 Executive Boulevard  
Rockville, MD 20892-9904  
Telephone: (301) 496-7815  
FAX: (301) 402-1037

Direct inquiries regarding fiscal matters to:

Mr. Robert Hawkins  
Grants Management Branch  
National Cancer Institute  
Executive Plaza South, Room 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800, ext. 13

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.396. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

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# NIH GUIDE

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National Institutes of Health

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 29  
August 14, 1992

RICHARD W. HURRY

920 MILL FOREST DRIVE  
GAITHERSBURG MD 20878-9000

701167  
5130 LEAS

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*



LABORATORY ANIMAL SMALL RESEARCH GRANTSNIH GUIDE, Volume 21, Number 29, August 14, 1992

P.T. 34; K.W. 1002002, 0710035

National Center for Research Resources

This is to advise potential applicants that the National Center for Research Resources (NCRR) Comparative Medicine Program will henceforth accept Small Research Grant (R03) applications at any of the three standard annual application receipt dates (February 1, June 1, and October 1). Such applications have previously been accepted only for the February 1 deadline. These awards are limited to \$25,000 direct costs and only one year of support. They are intended to provide support for pilot projects, testing of new techniques, and feasibility studies of innovative research in the areas of laboratory animal biotechnology, normative biology, disease, welfare, and model development.

## INQUIRIES

Further information concerning these awards and updated guidelines for applicants may be obtained by sending two self-addressed mailing labels to:

Comparative Medicine Program  
National Center for Research Resources  
Westwood Building, Room 857  
Bethesda, MD 20892  
Telephone: (301) 496-5175

TERMINATION OF SMALL GRANTS PROGRAM FOR BIOETHICS AND CLINICAL DECISION MAKING RESEARCHNIH GUIDE, Volume 21, Number 29, August 14, 1992

P.T.

National Center for Nursing Research

The National Center for Nursing Research (NCNR) announces plans for the orderly phase out and termination of its small grants program for bioethics and clinical decision making research. All non-competing commitments for future year support made to current grantees will continue to be honored, as will applications selected for award that have completed the review process in FY 1992. No new applications will be accepted for review for FY 1993.

The NCNR continues to encourage potential investigators to use alternative grant mechanisms, such as the R01 and R29, for addressing bioethical and clinical practice studies. Training in bioethics for nurses also continues to be encouraged.

## INQUIRIES

For additional information and for questions concerning this notice, contact:

Dr. Barbara Pillar  
Nursing Systems Branch  
National Center for Nursing Research  
Westwood Building, Room 754  
Bethesda, MD 20892  
Telephone: (301) 496-0523  
FAX: (301) 402-2402

NIDCD - INSTITUTIONAL NATIONAL RESEARCH SERVICE AWARDSNIH GUIDE, Volume 21, Number 29, August 14, 1992

P.T.

National Institute on Deafness and Other Communication Disorders

The National Institute on Deafness and Other Communication Disorders announces a new receipt and review cycle for Institutional National Research Service Award (T32) applications. Beginning in 1993, such applications will be accepted and reviewed only once a year. For this annual cycle, applications will be accepted only for the May 10 deadline, and will receive initial review in October/November, followed by National Advisory Council review in January. Annual funding decisions will be made shortly following the January Council meeting. Most Institutional National Research Service Awards have had, and will continue to have, July 1 start dates.

For more specific information and guidance, contact:

Daniel A. Sklare, Ph.D.  
Program Administrator  
Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Suite 400B  
Bethesda, MD 20892  
Telephone: (301) 402-3461

NOTICES OF AVAILABILITY (RFPs AND RFAs)

CENTERS OF RESEARCH ON APPLIED GERONTOLOGY

NIH GUIDE, Volume 21, Number 29, August 14, 1992

RFA AVAILABLE: AG-93-02

P.T. 04; K.W. 0710010, 0404000, 0417000

National Institute on Aging

Letter of Intent Receipt Date: October 2, 1992

Application Receipt Date: November 18, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

PURPOSE

This announcement seeks to establish Centers of Research on Applied Gerontology. The Centers' purpose will be to facilitate the process of translating basic behavioral and social research theories and findings into practical outcomes that will benefit the lives of older people. They will focus on strategies to improve quality of life, enhance productivity, and minimize the need for care.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priorities. This RFA, Centers of Research on Applied Gerontology, addresses several priority areas including chronic disabling conditions, physical activity and fitness, violent and abusive behavior, and unintentional injuries as they relate to older people. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

ELIGIBILITY REQUIREMENTS

Domestic public and private, for-profit and non-profit institutions and organizations are eligible to apply in response to this RFA, provided that some member of the proposed research team at the institution has recently received grant or contract funds or is currently active in research through an external peer-reviewed process in the three years preceding the date of application. Applications from women and minority investigators and institutions are encouraged. Awards will not be made to foreign institutions.

MECHANISM OF SUPPORT

The support mechanism for these Centers will be the specialized center (P50) mechanism. Such awards cover a spectrum of activities that comprise a multidisciplinary attack on a particular problem area. A maximum of five years of support may be requested. At that time funds may be available for competitive renewal of the Centers. All current policies and requirements that govern the research grant programs of the NIH will apply to grants awarded in connection with this RFA.

Special Terms of Awards applying to projects funded in response to this RFA are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS grants administrative regulations at 45 CFR Part 74, and other HHS, PHS, and NIH grants administration policies. Awardees will maintain custody of and primary rights to their data developed under their awards, subject to Government rights of access, consistent with current HHS, PHS, and NIH policies.

FUNDS AVAILABLE

An estimated \$3,000,000 will be made available in Fiscal Year 1993 for support of awards made under this RFA. It is expected that up to six awards will be made at a maximum of \$400,000 direct costs per award for the first year. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Awards pursuant to the RFA are contingent upon the availability of funds for this purpose. Commitment from the applicant will be considered in making final awards.

RESEARCH OBJECTIVES

Researchers are encouraged to seek funding to apply the theories, paradigms, and methodology of the behavioral and social sciences in order to address practical problems of late middle aged and older people at work, in the

home, in transportation, in health care, or in other areas of concern to the population. The focus of this initiative is on translating encouraging research results obtained in laboratory and other scientific settings into practical benefits for older adults. The organizing principle behind each Center should reflect this aim of establishing a pattern of research translation from basic research to practical outcome.

The individual projects that are part of the Center should have as the goal a practical end-point---improvement in some indicator or indicators of functioning in these different environments. Improvements in aspects of behavioral indicators relevant to the practical domain (e.g., laboratory measures of cognitive functioning, health status, or subjective well-being) may be considered interim goals of the research strategy. However, the end-point is improvement in functioning in the practical domain itself. Thus the goal will not only be confirming a theory or discovering a new effect (though these may be expected from well-designed studies addressing practical problems).

One highly desirable feature of the Centers will be a focus on special populations of older people. Growth in size of minority older populations has been, and will continue to be, substantial. The oldest old remain the population at greatest risk for dependency. Older adults who have been identified as retarded face particular problems in later life. Poor older adults in rural areas have severely limited access to health care and general services. These and other special populations who have pressing needs warrant attention from researchers in aging.

#### SPECIAL REQUIREMENTS

##### Annual Meeting

Investigators are encouraged to request funds to travel once each year to meet with the other investigators who are funded through this RFA. The meetings will be held at the NIH, Bethesda, MD. The purpose of the meetings is to have investigators working in the same general area share information about research methods and findings. Applicants should include a statement in the application indicating a willingness to participate in such meetings and to cooperate with other researchers in the exchange of data, materials, and ideas.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by October 2 1992, a letter of intent that includes identification of other participating investigators and institutions and a descriptive title. The NIA requests such letters only for the purpose of providing an indication of the number and scope of applications to be received and, therefore, usually does not acknowledge their receipt. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

The letter of intent is to be sent to Dr. Robin A. Barr at the address under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. This form is available in the applicant institution's office of sponsored research or business office and from the Office of Grants Inquiries, National Institutes of Health, Room 449, Westwood Building, Bethesda, MD 20892-9912, telephone (301) 496-7441.

#### REVIEW CONSIDERATIONS

Upon receipt, the Division of Research Grants will review applications for completeness and NIA staff will review applications for responsiveness. Applications that are incomplete, nonresponsive to this RFA, or exceed the annual direct cost limit of \$400,000 (including total costs for sub-contracts) will be returned to the applicant without further consideration. The NIA will withdraw from further competition those applications judged by triage to be noncompetitive for award and notify the applicant and institutional official. Applications judged to be competitive will undergo further scientific merit review by an initial review group within the NIA. This review may involve an applicant interview or site visit. The second level of review will be provided by the National Advisory Council on Aging.

The most important criterion for scientific merit review will be the proposed Center's demonstrated potential to act as a conduit between basic behavioral and social research and applied outcomes. Both the evidence of past involvement in related research and the specific plans for seeking applied outcomes described in the application will be considered part of that potential. A related and important criterion concerns the proposed Center's ability to address the needs of special populations of older people who are identified as having particularly pressing concerns.

#### INQUIRIES

Inquiries concerning this RFA are encouraged in order to clarify issues or questions. The RFA may be obtained from the program contact listed below who will also answer questions on programmatic issues related to the RFA:

Dr. Robin A. Barr  
Behavioral and Social Research  
National Institute on Aging  
Gateway Building, Room 2C234  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-3136  
FAX: (301) 402-0051  
E-mail: Barr@NIHNIAGW.BITNET

Questions on fiscal matters should be directed to:

Ms. Linda Whipp  
Grants and Contracts Management  
National Institute on Aging  
Gateway Building, Room 2N212  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-1472

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.866. Awards are made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### CLINICAL CORE CENTERS FOR PREVENTIVE AND OPERATIVE DENTISTRY

NIH GUIDE, Volume 21, Number 29, August 14, 1992

RFA AVAILABLE: DE-92-04

P.T. 04; K.W. 0785040, 0715148, 0745027

National Institute of Dental Research

Letter of Intent Receipt Date: October 31, 1992  
Application Receipt Date: December 3, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute of Dental Research (NIDR) invites applications for the support of Clinical Core Centers for Preventive and Operative Dentistry (CCCPD). The CCCPDs are intended to serve as focal points to strengthen the Nation's research capability in clinical oral health and to facilitate the development of new approaches to the prevention and treatment of dental caries and failed restorations. Center goals will include: (1) developing state-of-the-art clinical research capacity through shared resources and facilities (core units) that strengthen and expand relevant clinical research; (2) providing a nucleus around which additional clinical studies funded through government and private sources can be conducted; and (3) facilitating and stimulating clinical research to improve oral health in children, adults, senior citizens, and others at high risk for caries including those with systemic diseases or oral conditions that increase the risk for recurrent disease.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas, and to "Oral Health 2000," a major collaborative initiative between the PHS and professional and private research organizations to improving oral health in the adult and elderly population groups in the U.S.A. This RFA, Clinical Core Centers for Preventive and Operative Dentistry, is related to the priority area of reducing health disparities among Americans by improving oral health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

This competition is open to domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the federal Government. Foreign organizations are not eligible to apply, however, domestic applications may include international components.

Although an application must be submitted from a single institution, it may include consortia arrangements with other institutions, provided these arrangements are clearly delineated and formally and officially confirmed by signed statements from the responsible officials of each institution. Applicant institutions must provide clear evidence of having a suitable clinical research base to assure appropriate utilization of the added resources which NIDR would provide through the CCCPD. This must include meritorious ongoing clinical research projects and/or the capability to develop such clinical research, accompanied by firm funding commitments that ensure that appropriate clinical research projects will be active at the time of a CCCPD award.



## MECHANISM OF SUPPORT

The CCCPODs will be supported by the National Institutes of Health (NIH) Center Core Grants (P30). Clinical Core Center applications funded under this RFA will be supported for a period of five years, commencing as early as September 1, 1993. This RFA is for a single competition with a receipt date of December 3, 1992. Subsequent support will be contingent upon program needs and availability of funds.

In addition to support for pilot or feasibility projects, support will be provided for core resources, the sharing of which will facilitate the total research effort. Each core unit must be utilized by at least two projects. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant.

## FUNDS AVAILABLE

Applicants may request up to \$300,000 in direct costs for the first year. If indirect costs are assigned to a subcontract and counted as direct costs, the direct cost maximum of \$300,000 may be exceeded by the amount of the indirect costs assigned to the subcontract. Budget increases of no more than four percent per year may be requested for each of the subsequent four years. The NIDR expects to commit up to \$0.9 million to fund applications submitted in response to this RFA. It is anticipated that one or two awards will be made, however, this funding level is contingent upon the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIDR, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

The Centers are intended to serve as focal points for strengthening the nation's oral health clinical research capability, enhancing clinical decision-making, and facilitating the development of new approaches for caries diagnosis, prevention, and treatment in the light of recent knowledge of caries etiology and pathogenesis.

The overall intent of this RFA is to attract clinical researchers and clinicians with experience in dental materials science, molecular biology, biochemistry, pulp biology, and clinical preventive and operative dentistry, as well as those involved in the prevention, diagnosis and treatment of dental caries. The research will focus on multi-disciplinary approaches to early diagnosis and treatment of caries, making the distinction between caries as a disease and caries as a lesion. Particular emphasis is placed on the assessment of the presence and severity of infection through identification of microbiological and biochemical markers and prompt treatment prior to evidence of clinical symptoms.

The research also should focus on the full range of treatments including non-operative interventions such as the use of antibacterial and remineralization procedures, minimal intervention such as preventive resin restorations, and different types of other restorations needed for the treatment of carious lesions. Particular attention should be paid to the development of optimal cavity preparations for different types of restorative materials. The principle of cavity preparations must be based on the premise of maintaining tooth structure to prevent the need for large restorations and more complex sequelae. The research should include development and testing of maintenance and health promotion programs and studies on why restorations fail.

Each Center must include a minimum of three core units including an administrative core, a biostatistics core, and one or more cores directly related to ongoing and planned oral health clinical research. Examples of the latter core units include: diagnostic cores to develop methods and/or instrumentation to detect early signs or markers of oral disease or dysfunction and to monitor the efficacy of treatments; laboratory cores to provide resources to carry out adjunct studies on patient or healthy populations, and unique clinical facilities to facilitate research that cannot be carried out in conventional health-care settings (e.g., mobile units or work-site units).

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by October 31, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of this RFA. Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains is helpful in planning for the timely review of applications. It allows Institute staff to estimate the potential review workload and to avoid conflict of interest in review.

The letter of intent is to be addressed to Joyce A. Reese, D.D.S., M.P.H. at the address under INQUIRIES.

## APPLICATION PROCEDURES

Applications are to be prepared on form PHS 398 (rev. 9/91), Application for PHS Grant, which may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441, and from most institution's Office of Research and Sponsored Programs.

Applications must be received by December 3, 1992. If an application is received after that date, it will be

returned to the applicant without review.

#### REVIEW CONSIDERATIONS

Applications will be evaluated by a special review committee, convened by the NIDR Scientific Review Branch. Prior to the initial review, a triage mechanism may be used to screen applications that are noncompetitive to the RFA. Applicant interviews or site visits may not be conducted, and the application should therefore be complete. Secondary review will be conducted by the National Advisory Dental Research Council. Applications must be received by December 3, 1992, so they can be reviewed and considered for funding in Fiscal Year 1993. Applications judged to be noncompetitive or nonresponsive to the RFA, and those received after December 3, 1992 or exceeding the budget limitation will be returned without review. Waivers of the receipt deadline and budget limitation will not be granted.

#### INQUIRIES

Written and telephone request for the RFA and an opportunity to clarify any issues or questions from potential applicants are welcome.

Direct request for the RFA and inquiries regarding programmatic issues to:

Joyce A. Reese, D.D.S., M.P.H.  
Director, Biomaterials, Pulp Biology and Dental Implants Program  
National Institute of Dental Research  
Westwood Building, Room 505  
Bethesda, MD 20892-4500  
Telephone: (301) 496-7884  
FAX: (301) 496-4180

Direct inquiries regarding fiscal matters to:

Ms. Theresa Ringler  
Chief, Grants Management Section  
National Institute of Dental Research  
Westwood Building, Room 518  
Bethesda, MD 20892  
Telephone: (301) 496-7437  
FAX: (301) 402-1260

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.1212. Awards will be made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SUPPLEMENTS FOR UNDERGRADUATE RESEARCH EXPERIENCE PROGRAM

NIH GUIDE, Volume 21, Number 29, August 14, 1992

P.T.

RFA: GM-92-003

National Institute of General Medical Sciences

Application Receipt Date: November 6, 1992

#### PURPOSE

The National Institute of General Medical Sciences (NIGMS) announces a pilot program, the Supplements for Undergraduate Research Experience (SURE) Program, to provide supplements to NIGMS grants to enable Principal Investigators (PI) to support undergraduate students for a 10-week summer research experience in their laboratories. The purpose of the program is to attract talented students to careers in the biomedical sciences by giving them a hands-on research experience at a critical point in their academic careers.

#### ELIGIBILITY REQUIREMENTS

PIs at domestic institutions who hold an active Research Project (R01), First Independent Research Support and Transition (FIRST) (R29), Method to Extend Research in Time (MERIT) (R37), Program Project (P01), or Center (P50) grant from the NIGMS are eligible to submit a request for an administrative supplement. Recipients of Academic Research Enhancement Awards (AREA) (R15) and Small Business Innovative Research (SBIR) (R43 and R44) grants are not eligible, nor are PIs at foreign institutions. In all cases, the parent grant must have support remaining through the period of the proposed SURE award.

It is expected that each parent grant, including Program Projects and Centers, will support only one undergraduate student through this program. Award of an administrative supplement to support a minority undergraduate student under the Research Supplements for Underrepresented Minorities program or a disabled undergraduate student under the program of Research Supplements to Promote the Recruitment of Individuals with Disabilities into Biomedical Research Careers in no way precludes an award to the PI through the SURE Program.

Support will be provided through supplements made to active R01, R29, R37, P01, and P50 grants funded by the NIGMS. This RFA is a one-time solicitation.

Successful applicants for supplements will be notified in February 1993 in order to provide sufficient time to recruit talented students. The supplement is not to exceed \$6.00 per hour for salary plus \$125 per month for supplies for a period of 10 weeks. Equipment may not be purchased from these funds. Applicable indirect costs will be provided. Supplemental funds will be restricted to the purpose described in this announcement. Recipients of supplements must submit appointment forms (PHS 2271) to the NIGMS. Students who are supported by SURE awards will be designated "NIGMS Summer Scholars" and will receive certificates at the completion of their research experience.

#### FUNDS AVAILABLE

It is estimated that the NIGMS will award up to 250 SURE awards. This level of support is dependent on the receipt of a sufficient number of applications of high merit. Although this program is provided for in the financial plans of the NIGMS, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The NIGMS is strongly committed to supporting research training in the biomedical sciences through its institutional training grants and individual fellowships awarded under the National Research Service Award (NRSA) Act. The NIGMS recognizes that to maintain the success of its training programs, talented undergraduate students must continue to be attracted to the biological sciences and related areas, such as chemistry, physics, and mathematics. Often, however, promising undergraduates, particularly at large, research-intensive universities, are deterred from pursuing science majors because of a lack of opportunity for personal participation in research at a critical stage in their academic careers.

The SURE Program will make administrative supplements to NIGMS research grants to enable PIs to provide support for undergraduate students who participate in research in their laboratories for the summer. Supplements will be awarded for support during the summer of 1993, and it is hoped that institutional and other sources of support will enable interested students to continue the research experience beyond the initial summer.

Supplements to NIGMS research grants are designed to provide beginning undergraduate students who have not yet begun their junior year with a summer research experience. The proposed research must be an integral part of the approved ongoing research supported by the parent grant. As part of this research experience, the student must be given the opportunity to interact with scientists and graduate students in the laboratory, to contribute intellectually to the research, and to enhance research skills and knowledge in the particular area of biomedical science. In addition, the PI must demonstrate an ability and a willingness to serve as a supportive mentor and a role model in encouraging interest in a career in biomedical research. Although it is understood that other members of the laboratory will be involved in the student's training, it is expected that the PI will be responsible for serving as the primary mentor. In particular, it is expected that the PI will discuss with the student the ongoing research in the laboratory and its broader scientific context, appropriate laboratory practices and scientific conduct, appropriate use of human subjects and animals, if applicable, and career options. Supplemental awards will be consistent with the goal of strengthening the existing research program. Awards will be made according to the policies and provisions stated in this announcement.

Students are expected to devote an equivalent of 10 weeks of full-time effort to the research project.

#### SPECIAL REQUIREMENTS

By acceptance of a supplement, the PI agrees to provide the NIGMS, as part of the next progress report (non-competing, competing, or final), with an evaluation of the student's accomplishments during the program. In addition, the PI is responsible for ensuring that the student submit a one to two page report which should include both a description of the research project and results obtained and an evaluation of the research experience and an assessment of its impact on career goals. This report should be submitted to the NIGMS no later than September 15, 1993.

#### APPLICATION PROCEDURES

All requests for supplements must be received by November 6, 1992. In making requests, the grantee institution, on behalf of the PI of the parent grant, must submit four copies of the application, including a signed original, directly to:

Office of the Associate Director for Program Activities  
National Institute of General Medical Sciences  
Westwood Building, Room 940  
5333 Westbard Avenue  
Bethesda, MD 20892

The request for a SURE award must include the following:

o A completed face page (with appropriate signatures) from grant application form PHS 398 (rev. 9/91). This form is available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. Include on line 1 the title and grant number of the parent grant and specify on line 2a (Response to Specific Request for Applications or Program Announcement) "Supplement for Undergraduate Research Experience."

o A brief description (maximum of three pages), prepared by the PI of the parent grant, that includes:

(a) the PI's plans for mentoring, training, and advising the student. It is NOT necessary to have identified a student for support at the time of submission of the request, but, if a student has not been identified, some indication should be given of the plans to recruit, the criteria for selection of a student, and the likelihood of success;

(b) plans for the student's research experience and a discussion of the student's role in relation to the research supported by the parent grant;

(c) expectations for how the research experience will foster the research capabilities and scientific interests of the student;

(d) a proposed budget entered on the budget pages from the grant application form PHS 398; and

(e) documentation, if applicable, that the proposed research experience was approved by the Institutional Animal Care and Use Committee (IACUC) or the Human Subjects Review Board (IRB) of the grantee institution.

#### REVIEW CONSIDERATIONS

The staff of the NIGMS will review requests for supplements using the following general criteria:

- o Adequacy of the plan for the proposed research experience of the student;
- o Evidence that the experience will enhance the research potential, knowledge, and/or skills of the undergraduate and his/her interest in biomedical science;
- o Evidence that the activities of the student will be an integral part of the project;
- o The suitability of the research environment; and
- o The commitment of the PI and the grantee institution to promote and support undergraduate research. A strong indication of the PI's commitment is a demonstration of past mentorship of undergraduates.

#### AWARD CRITERIA

It is hoped that many of the students supported under the SURE Program will be able to continue their research experiences beyond the 10-week period with institutional support. A commitment of this sort from the PI and the grantee institution would be viewed favorably in making awards.

#### INQUIRIES

Principal Investigators interested in applying for this program may contact the program administrator whose name appears on the Notice of Grant Award or:

Michael Martin, Ph.D.  
Deputy Associate Director, Office of Program Activities  
National Institute of General Medical Sciences  
Westwood Building, Room 938  
Bethesda, MD 20892  
Telephone: (301) 496-7063

Inquiries regarding fiscal matters are to be directed to the grants management specialist whose name appears on the Notice of Grant Award or:

Ms. Ruth Monaghan  
Deputy Grants Management Officer  
National Institute of General Medical Sciences  
Westwood Building, Room 953  
Bethesda, MD 20892  
Telephone: (301) 496-7746

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.821, 93.859, 93.862, 93.863. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.



RESEARCH CAREER DEVELOPMENT IN MYCOBACTERIUM TUBERCULOSIS

NIH GUIDE, Volume 21, Number 29, August 14, 1992

PA NUMBER: PA-92-96

P.T. 34; K.W. 0715125, 0715165, 1002008, 0710070, 0740075, 0745020

National Institute of Allergy and Infectious Diseases

## PURPOSE

The Department of Health and Human Services (DHHS) National Action Plan to Combat Multidrug-Resistant Tuberculosis (April 1992) has listed the training of tuberculosis researchers as a high priority item necessary to achieve tuberculosis control. Individuals trained as physician-investigators and basic scientists are essential to expansion of high quality research programs in the area of tuberculosis. There is an urgent need to promote research training in basic and clinical aspects of tuberculosis including improved diagnosis, molecular biology, therapeutics, patient compliance, immunology, and vaccine development. Many laboratory techniques for the diagnosis of tuberculosis and for the identification of drug resistance were developed in the 1950s and 1960s. Although more accurate, rapid, and sophisticated methods are available, they have not been implemented for tuberculosis. The increasing incidence of both tuberculosis and drug-resistant tuberculosis makes it imperative to apply current technologies to the fullest capacity.

This Program Announcement (PA) emphasizes the commitment of the National Institute of Allergy and Infectious Diseases (NIAID) to support Clinical Investigator Awards (K08), Physician Scientist Awards (K11), and Research Career Development Awards (K04) to increase the number of biomedical investigators conducting high-quality research in the area of Mycobacterium tuberculosis (Mtb). The NIAID encourages eligible individuals, including underrepresented minorities and women, to submit applications.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Research Career Development in Mycobacterium Tuberculosis, is related to the priority areas of immunization and infectious diseases, and HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9935 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

The PSA-K11 award is designed to encourage newly trained clinicians to develop independent research skills and experience in a fundamental science. Applicants for the PSA must hold an M.D. or other health professional degree. Ordinarily, candidates holding both a medical degree and a Ph.D. degree in the biomedical sciences are ineligible.

The CIA-K08 award seeks to provide clinically trained individuals with demonstrated aptitude in research to develop into independent investigators. Applicants for the K08 award must hold an M.D. or other health professional degree, have had three to five years of clinical and research postdoctoral experience by the projected start of the award and not have been a Principal Investigator on a Public Health Service-supported research project grant (R01, R29, R15).

The RCDA-K04 award is designed to foster the development of young scientists with outstanding research potential for careers of independent research in health related sciences. The salary support provided is intended to allow release time from most of the teaching, clinical, and administrative duties to permit nearly full time involvement in research efforts. Applicants for the RCDA must hold a doctoral degree or equivalent and have at least five years postdoctoral research experience which can include two years as the Principal Investigator of a peer reviewed research grant, prior to the requested beginning date of the award.

## MECHANISMS OF SUPPORT

Each of the career development mechanisms is tailored to a particular stage of an investigator's career. Existing mechanisms supported by the NIAID include: the Physician Scientist Award (PSA-K11), the Clinical Investigator Award (CIA-K08), and the Research Career Development Award (RCDA-K04). Physician investigators are encouraged to use the PSA and CIA to develop expertise in basic and clinical research. Only U.S. citizens or non-citizens lawfully admitted for permanent residence at the time of application are eligible to apply. The distinguishing features of each of the "K" mechanisms are summarized above. The booklet, The K Awards, is available from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892-9912, (telephone: (301) 496-7441).

## SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application. All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### RESEARCH OBJECTIVES

Studies that are encouraged include, but are not limited to, the following research areas:

- o Basic Biology: Studies on the growth, physiology, biochemistry, genetics, and molecular biology of Mtb.
- o Pathogenesis: Clinical and basic research on the pathogenesis of Mtb including physiology, biochemistry, and structural biology; identification and characterization of virulence factors; genetic exchange, and the development of physical and genetic maps; mechanisms of drug resistance; role of cytokines in disease progression; and the mechanism of latency and reactivation of infection, especially characterization of the cellular and molecular components of the immune-mediated mechanisms involved in the development of active and latent disease and in protection.
- o Improved Diagnostic Procedures: Development and evaluation of new technologies to rapidly and reliably diagnose tuberculosis and identify drug susceptibility patterns. Research in further innovation and application of diagnostic tests to distinguish between active and latent tuberculosis in patients with compromised immune systems.
- o Drug Discovery and Development: Development of new in vitro assays, culture systems, and animal models to assess the safety and efficacy of potential compounds to treat tuberculosis. Research in the development and evaluation of new drugs and modalities to treat and prevent multi-drug resistant tuberculosis. Research to reduce the duration of therapy required to treat drug-susceptible infections. Research on timed controlled-release drugs and the administration or means to increase compliance with therapy.
- o Vaccine Development: New and improved vaccines to prevent Mtb infection. Development of novel vaccine vectors. Research on the regulation of responses by immunomodulators and identification of the antigens involved in protection. Development of animal models to correlate immune responses with protection.

#### APPLICATION PROCEDURES

Application receipt dates for all competing career development awards (K series) are February 1, June 1, and October 1. Institute assignment decisions will be governed by the program considerations as specified in the PHS Referral Guidelines. Earliest possible funding dates are approximately ten months after the receipt dates. The special instructions for the PSA and CIA are found in the publication entitled "The K Awards," revised October 1991. Application form PHS 398 (rev. 9/91) and "The K Awards" are available from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892-9912. Applications submitted in response to this program announcement must be identified by typing "PA-92-96, Research Career Development In Mycobacterium Tuberculosis" on line 2a of the face page of the PHS 398 form that is available from the applicant institution's office of sponsored research and from the Office of Grants Inquiries, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed activity. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator must be included with the application.

#### REVIEW CONSIDERATIONS

Applications in response to this announcement will receive initial peer review on the basis of standard NIH review criteria and guidelines. Applications for the Clinical Investigator Award (K08) and the Physician

Scientist Award (K11) will be reviewed for scientific review groups (SRGs) convened by the concerned institute. Applications for Research Career Development Awards (K04) will be reviewed for scientific merit by initial review group(s) (IRGs) convened by the Division of Research Grants, NIH. Applicants are referred to the NIH brochure, The K Awards (October 1991 edition), which details the qualifications, eligibility, etc., for the K08, K11, and K04 candidates, as well as the review criteria. This brochure should be available at the institution's business office, or a copy may be requested from the Grants Inquiries Office, Division of Research Grants, National Institutes of Health, Bethesda, MD 20892, telephone (301) 496-7441. Award criteria will be the overall merit of the application as determined by the IRG, relevance of the application to the research objectives as outlined in this PA, and availability of funds.

#### AWARD CRITERIA

The award of grants pursuant to this announcement is contingent upon availability of appropriated funds. The following criteria will be used in making funding decisions: overall merit of the proposed project as determined by peer review, availability of funds, relevance to the research priorities of the awarding institute, and program balance among research areas of the announcement.

#### INQUIRIES

For further information about NIAID career development awards, contact:

Dr. Milton J. Hernandez  
Director, Office of Science Training and Manpower Development  
National Institute of Allergy and Infectious Diseases  
Solar Building 4C-10  
6003 Executive Blvd.  
Bethesda, MD 20892  
Telephone: (301) 496-7291

For inquiries regarding fiscal and business matters, contact:

Ms. Barbara A. Huffman  
Special Assistant for Operations  
Grants Management Branch  
Director of Extramural Affairs  
National Institute of Allergy and Infectious Diseases  
Solar Building 4C-26  
6003 Executive Blvd.  
Bethesda, MD 20892  
Telephone: (301) 496-7075

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.855, Allergy, Immunology and Transplantation Research, and No. 93.856, Microbiology and Infectious Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### DEVELOPING AND IMPROVING INSTITUTIONAL ANIMAL RESOURCES

NIH GUIDE, Volume 21, Number 29, August 14, 1992

PA NUMBER: PA-92-97

P.T. 34; K.W. 1002002

National Center for Research Resources

Application Receipt Date: October 1, 1992

#### PURPOSE

The National Center for Research Resources (NCRR) assists institutions in developing, modernizing, and improving animal resources for biomedical research and research training by awarding research and resource grants. Animal resource improvement grants (G20) are awarded for this purpose and to assist institutions in complying with the provisions of the Animal Welfare Act and Public Health Service (PHS) policies related to the care and use of laboratory animals. Requests are limited to alterations and renovations (A&R) and to purchases of major animal resource equipment (with a unit value of at least \$1,000). Support for new construction, including completion of shell space, is not authorized. Projects may address improvement of animal facilities and related activities, including centralized experimental surgical facilities, diagnostic laboratories, and transgenic animal resources.

#### ELIGIBILITY REQUIREMENTS

Any domestic public or private institution, organization, or association with one or more research projects supported by the PHS that involve the use of laboratory animals is eligible to apply. Institutions and commercial firms providing only services or products and without a clearly defined animal related research component are not eligible to apply. Also, this program will not support requests for equipment used for teaching purposes and for housing non-research animals. Applicants may not submit more than one application



or apply for other NCRR support for developing and improving institutional animal resources in the same Federal fiscal year.

There is a separate program and guidelines for animal facility improvement grant applications from small research institutions receiving less than \$1,000,000 (direct costs) of PHS support for research projects during the most recently completed Federal fiscal year (refer to PA-92-10 that was published in the NIH Guide for Grants and Contracts, Vol. 20, No. 39, October 18, 1991).

#### MECHANISM OF SUPPORT

The mechanism available for the support of improvement projects is the Grant for Repair, Renovation, and Modernization of Existing Research Facilities (G20). Requests are limited to A&R to improve existing laboratory animal facilities, allowable fees associated with the A&R project, and major resource equipment related to the improvement project, such as animal cage systems and cage washers. Equipment requests must have a manufacturer's unit value of at least \$1,000. Requests for basic general purpose equipment items for centralized surgeries, diagnostic laboratories, transgenic animal facilities, and other similar associated activities are allowable when well justified and integral to the proposed project. The total budget request for the improvement grant application and award is limited to a total of \$700,000 (direct costs), of which not more than \$500,000 may be used for alterations and renovations. Matching funds from non-Federal sources, equal to or exceeding one-half of the total award (\$2 Federal to \$1 non-Federal), are required.

#### RESEARCH OBJECTIVES

Animal resource improvement grants are awarded to assist biomedical research institutions in upgrading animal facilities and developing administratively centralized and uniformly effective programs of animal care. Another major objective is to assist institutions in complying, and maintaining compliance, with provisions of the Animal Welfare Act and PHS policies related to the care and use of laboratory animals.

#### APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398, "Application for Public Health Service Grant," (rev. 9/91) to the NIH Division of Research Grants. The single annual receipt date for applications in response to this announcement is October 1. Applications received by this deadline will receive February/March initial peer review, May/June review by the National Advisory Research Resources Council, and will have an earliest possible award date of July 1. Applications received after the October 1 deadline will be returned to the applicant without review.

The completed original application (signed original including appendices, if any) and three copies must be sent or delivered to:

Grant Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892-4500\*\*

Simultaneously, two additional copies (with appendices, if any) must be sent under separate cover to:

Scientific Review Administrator  
Comparative Medicine Review Committee  
Office of Review  
National Center for Research Resources  
Westwood Building, Room 10A16  
Bethesda, MD 20892-4500\*\*

Application forms (PHS 398) may be obtained from grantee business or sponsored projects offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892-4500, telephone: (301) 496-7441.

#### REVIEW CONSIDERATIONS

All applications will be reviewed for scientific and technical merit by an appropriate review committee managed by the Office of Review, NCRR. Second level review will be provided by the National Advisory Research Resources Council. Review of the applications will be based on scientific merit, technical soundness, and cost effectiveness.

#### AWARD CRITERIA

Applications will compete for available funds with all other applications assigned to the Comparative Medicine Program, NCRR. The following will be considered when making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Institutional assurance of non-federal matching funds
- o Availability of funds

#### INQUIRIES

Inquiries about specific improvement program guidelines and detailed instructions for application and other aspects of the program are encouraged and are to be directed to the following address (requests for guidelines must include two self-addressed mailing labels):



Director, Laboratory Animal Science Program  
Comparative Medicine Program  
National Center for Research Resources  
Westwood Building, Room 857  
5333 Westbard Avenue  
Bethesda, MD 20892-4500  
Telephone: (301) 496-5175  
FAX: (301) 480-0868

Questions regarding fiscal matters are to be directed to:

Mr. Paul Karadbil  
Supervisory Grants Management Specialist  
Office of Grants and Contracts Management  
National Center for Research Resources  
Westwood Building, Room 849  
Bethesda, MD 20892-4500  
Telephone: (301) 496-9840

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.306, Laboratory Animal Sciences and Primate Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78.410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SCIENTIST DEVELOPMENT AWARD FOR CLINICIANS

NIH GUIDE, Volume 21, Number 29, August 14, 1992

PA AVAILABLE: PA-92-98

P.T.

National Institute on Alcohol Abuse and Alcoholism  
National Institute on Drug Abuse  
National Institute of Mental Health

Application Receipt Dates: February 1, June 1, October 1

THE PROGRAM ANNOUNCEMENT (PA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE PA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, and the National Institute of Mental Health provide Scientist Development Awards for Clinicians to eligible applicants early in their careers who need additional supervised research experience to develop into independent scientists. These awards are intended to make it possible for investigators to engage in alcohol, drug abuse, and/or mental health related research on a full-time, long-term basis, and to stimulate recipient institutions to maintain and expand existing research programs or to establish new ones for studies in these areas.

Each funding component has different program goals and initiatives; therefore, potential applicants must contact the appropriate Institute office, listed below, prior to preparing an application to obtain the full Program Announcement (PA) and current information with regard to the Scientist Development Award.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Scientist Development Award For Clinicians, is related to the priority areas of mental health and disorders and alcohol and other drugs. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Eligible applicant institutions include public and private, non-profit and for-profit organizations and institutions engaged in alcohol, drug abuse, and/or mental health research that are located in the United States or its territories and possessions. These institutions apply on behalf of a qualified candidate who holds an earned doctorate. Women and minority candidates in particular are encouraged to apply.

An individual who has been a Principal Investigator on a Public Health Service (PHS) research grant or who has had equivalent research support is not eligible for this award. Recipients of PHS Small Grant Awards are an exception to this restriction and are eligible to apply. Persons who hold a position with firm salary support for full time research, or those with endowed chairs, are not eligible.

#### MECHANISM OF SUPPORT

The mechanism of support is the Scientist Development Award for Clinicians (K20), which is intended for persons

trained primarily as clinicians who show great promise for becoming researchers, but need supervised research experience to develop into independent investigators.

The essential elements of the K20 are the qualifications and potential of the candidate, an individualized, well thought-out career development and research plan, a dedicated, capable preceptor, and commitment on the part of the applicant institution to the development of the candidate. Documentation concerning each of these essential elements must be included in the K20 application.

The candidate must be a citizen or noncitizen national of the United States, or must have been lawfully admitted to the United States for permanent residence and must possess an Alien Registration Receipt Card (Form I-151 or I-551) at the time of an award. The candidate must have had no more than three years of research training or experience in the aggregate and must have had at least two years of postdoctoral clinical training or experience by the time the award is made.

**Period of Support:** The K20 is limited to a single period of five years.

**Salary Support:** The salary proposed must be consistent with the established salary structure for full-time, 12-month appointments at the grantee institution. The funding components' contribution to salary support is geared to the institution's base as follows: up to \$45,000 - 100 percent of institutional base; \$45,001 to \$60,000 - \$45,000; \$60,001 and over - 75 percent of institutional base, up to \$75,000. The grantee institution may supplement the contribution of the funding component up to a level consistent with the institution's salary scale. Fringe benefits are paid out of grant funds in the same proportion as the salary contribution.

**Allowance for Support Costs:** In addition to salary support, funds up to \$50,000 in the aggregate may be requested for each year to support research and/or career development activities. Applicants may request up to eight percent of direct costs for indirect costs.

#### RESEARCH OBJECTIVES

The NIAAA, NIDA, and NIMH provide an integrated Scientist Development Award Program that is made up of three types of awards: the Scientist Development Awards (K20, K21), the Research Scientist Development Award (K02), and the Research Scientist Award (K05). Together they provide a continuum of support for scientists at several stages of their careers. The K20 is designed for beginning individuals trained as clinicians showing great promise as researchers but requiring further supervised research experience to become outstanding independent investigators.

The K20 candidate should address a program of research relevant to the mission of the funding component. The trajectory of the candidate's development as a research scientist is of paramount importance in this program, and the intent is to assist a person with great potential to become an outstanding scientist, fully able to function as an independent investigator. An individual who holds a K20 grant is expected to apply for a small grant award, a First Independent Research Support and Transition (FIRST) award, a traditional research grant, or any other appropriate grant, providing that eligibility criteria for the other award(s) and terms and conditions of the K20 are met.

#### SPECIAL REQUIREMENTS

Individuals must devote full-time (at least 80 percent) to career development activities, supervised research, developing skill in research methods, or other research-related activities relevant to their career goals. Providing health care is acceptable only when it is necessary to maintain and enhance skills required for the conduct of research. Remuneration for clinical practice, consultation, or work related to the awardee's research program must be assigned to the grantee institution and may not be retained by the awardee.

**Use of PHS Research or Training Grant Funds Freed by a K20:** Funds budgeted in PHS-supported research or training grants for the salaries or fringe benefits of individuals, but freed as a result of a K20 award, may not be rebudgeted. Questions regarding leaves of absence, change of institution, or transfer of award should be addressed to appropriate staff of the PHS funding component.

**Concurrent Application:** The candidate for a K20 may not concurrently apply for any other PHS grant, nor may there be another application pending funding.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

Applications that involve human subjects are required to include minorities and both genders in study populations. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages.

#### APPLICATION PROCEDURES

Prospective applicants are advised to contact the relevant contact (see INQUIRIES) for a copy of the complete PA and for information regarding preapplication consultation and the application process. The research grant application kit form PHS 398 (rev. 9/91), is to be used in applying for the K20. These forms are available from institutional offices of sponsored research or their equivalent and from the offices listed under INQUIRIES.

Special instructions prepared for the K20 are included in the complete PA. The title and number of this PA, Scientist Development Award for Clinicians (PA-92-98), must be typed in Item 2a on the face page of the application form. Applications will be accepted on February 1, June 1, and October 1. Applications received after these receipt dates are subject to assignment to the next cycle or may be returned to the applicant, if so requested by the applicant.

An original and five copies of the completed and signed application are to be submitted to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Review procedures of K20 applications will be the customary system of dual review: evaluation for scientific and technical merit by an initial review group of the appropriate funding component consisting primarily of non-government scientific experts, followed by evaluation for policy and program relevance by the appropriate National Advisory Council. Only applications recommended for approval by the Council will be considered for funding. Applications will be reviewed for the candidate's potential to develop into a productive alcohol, drug abuse, and/or mental health researcher. Reviewers will consider: (1) the qualifications of the candidate including the suitability of the candidate relative to the eligibility criteria and purposes of the K20; (2) the soundness of the proposed career development plan; (3) the preceptor and institutional environment including the institution's commitment to the candidate's career; (4) the nature and scientific/technical merit of the research plan; and (5) the appropriateness of the budget. Detailed review criteria are listed in the full PA.

#### AWARD CRITERIA

The responsibility for award decision resides solely with authorized program staff of the funding components. The following criteria will be used in making award decisions: (1) overall merit of the application; (2) relevance of the application to the research priorities of the awarding component and program balance; and (3) availability of funds.

#### INQUIRIES

The full PA, which includes the Special Instructions for preparing K20 Applications, up-to-date policy guidelines, and the application forms, may be obtained from any of the following offices:

National Institute on Alcohol Abuse and Alcoholism  
OSAP National Clearinghouse for Alcohol and Drug Information  
P.O. Box 2345  
Rockville, MD 20847-2345  
Telephone: (301) 468-2600 or 1-(800)-729-6686

National Institute on Drug Abuse  
Grants Management Branch  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

National Institute of Mental Health  
Grants Awards and Operations Section  
Grants Management Branch  
5600 Fishers Lane, Room 7C-05  
Rockville, MD 20857  
Telephone: (301) 443-4414

Inquiries regarding grants management may be directed to the National Institute of Mental Health address given immediately above.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.271, 93.277, 93.281. Awards will be made under the authority of Section 301 of the Public Health Service Act, as amended (42 U.S.C. 241) and administered in accordance with the PHS grants policy statement revised October 1990. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SCIENTIST DEVELOPMENT AWARD

NIH GUIDE, Volume 21, Number 29, August 14, 1992

PA AVAILABLE: PA-92-99

P.T.

National Institute on Alcohol Abuse and Alcoholism  
National Institute on Drug Abuse  
National Institute of Mental Health

THE PROGRAM ANNOUNCEMENT (PA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE PA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH) provide Scientist Development Awards (SDA) to eligible applicants early in their careers who need additional supervised research experience to develop into independent



scientists. The SDA is also available to experienced investigators who require supervised research experience to enable them to switch fields. These awards are intended to make it possible for investigators to engage in alcohol, drug abuse, and/or mental health related research on a full-time, long-term basis, and to stimulate recipient institutions to maintain and expand existing research programs or to establish new ones for studies in these areas.

The NIAAA, NIDA, and NIMH each have different program goals and initiatives; therefore, potential applicants must contact the appropriate office, listed below, prior to preparing an application to obtain the full Program Announcement (PA) and current information with regard to the SDA.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Scientist Development Award, is related to the priority areas of mental health and disorders and alcohol and other drugs. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9935 (telephone 202/783-3238).

#### ELIGIBILITY REQUIREMENTS

Eligible applicant institutions include public and private, non-profit and for profit organizations and institutions engaged in alcohol, drug abuse, and/or mental health research that are located in the United States or its territories and possessions. These institutions apply on behalf of a qualified candidate who holds an earned doctorate. Women and minority candidates in particular are encouraged to apply.

An individual who has been a Principal Investigator on a Public Health Service (PHS) research grant or who has had equivalent research support is not eligible for the SDA. Recipients of PHS Small Grant Awards are an exception to this restriction and are eligible to apply. Experienced investigators applying for an SDA may previously have held a major PHS research grant or its equivalent; however, any such previous award must have been in an area substantially different from the research field in the SDA application. Persons who hold a position with firm salary support for full-time research, or those with endowed chairs, are not eligible.

#### MECHANISM OF SUPPORT

The mechanism of support is the Scientist Development Award (K21), which is intended for beginning basic scientists who show great promise but need supervised research experience to develop into independent investigators, and for experienced investigators requiring supervised research in order to switch fields.

The essential elements of the SDA are the qualifications and potential of the candidate, an individualized, well thought-out career development and research plan, a committed, capable preceptor, and commitment on the part of the applicant institution to the development of the candidate. Documentation concerning each of these essential elements must be included in the SDA application.

The candidate must be a citizen or noncitizen national of the United States, or must have been lawfully admitted to the United States for permanent residence and must possess an Alien Registration Receipt Card (Form I-151 or I-551) at the time of an award. The candidate must have had the equivalent of at least two years of postdoctoral research training or experience by the time the award is made.

Period of Support: The SDA is limited to a single period of five years. Experienced investigators switching fields may request support for a period of one to five years.

Salary Support: The salary proposed must be consistent with the established salary structure for full-time, 12-month appointments at the grantee institution. The funding component contribution to salary support is geared to the institution's base as follows: up to \$45,000 - 100 percent of institutional base; \$45,001 to \$60,000 - \$45,000; \$60,001 and over - 75 percent of institutional base, up to \$75,000. The grantee institution may supplement the funding component contribution up to a level consistent with the institution's salary scale. Fringe benefits are paid out of grant funds in the same proportion as the salary contribution.

Allowance for Support Costs: In addition to salary support, funds up to \$50,000 in the aggregate may be requested for each year to support research and/or career development activities. Applicants may request up to eight percent of direct costs for indirect costs.

#### RESEARCH OBJECTIVES

The NIAAA, NIDA, and NIMH provide an integrated Scientist Development Award Program that is made up of three types of awards: the Scientist Development Awards (K20, K21), the Research Scientist Development Award (K02), and the Research Scientist Award (K05). Together they provide a continuum of support for scientists at several stages of their careers. The SDA is designed for beginning individuals showing great promise as researchers but requiring further supervised research experience to become outstanding independent investigators. It may also be utilized by established investigators seeking to make significant changes in their research fields.

The SDA candidate must address a program of research relevant to the mission of the funding component. The trajectory of the candidate's development as a research scientist is of paramount importance in this program, and the intent is to assist a person with great potential to become an outstanding scientist, fully able to function as an independent investigator. An individual who holds a SDA grant is expected to apply for a small grant award, a First Independent Research Support and Transition (FIRST) award, a traditional research grant, or any other appropriate grant, providing that eligibility criteria for the other award(s) and terms and conditions of the SDA are met.



## SPECIAL REQUIREMENTS

Individuals must devote full-time (at least 80 percent) to career development activities, supervised research, developing skill in research methods, or other research-related activities relevant to their career goals. Providing health care is acceptable only when it is necessary to maintain and enhance skills required for the conduct of research. Remuneration for clinical practice, consultation, or work related to the awardee's research program must be assigned to the grantee institution and may not be retained by the awardee.

### Use of PHS Research or Training Grant Funds Freed By An SDA

Funds budgeted in Institute-supported research or training grants for the salaries or fringe benefits of individuals, but freed as a result of an SDA award, may not be rebudgeted. Questions regarding leaves of absence, change of institution, or transfer of award should be addressed to the appropriate staff of the funding component.

### Concurrent Application

The candidate for an SDA may not concurrently apply for any other PHS grant, nor may there be another application pending funding.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

Applications for SDAs that involve human subjects are required to include minorities and both genders in study populations. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages.

## APPLICATION PROCEDURES

Prospective applicants must contact the relevant office (see INQUIRIES) for a copy of the complete PA and for information regarding preapplication consultation and the application process. The research grant application kit form PHS 398 (rev. 9/91), is to be used in applying for the SDA. These forms are available from institutional offices of sponsored research and from the offices listed under INQUIRIES.

Special instructions prepared for the SDA are included in the complete PA. The title and number of this PA, Scientist Development Award (PA-92-99), must be typed in Item 2a on the face page of the application form. Applications will be accepted on February 1, June 1, and October 1. Applications received after these receipt dates are subject to assignment to the next cycle or may be returned to the applicant if so requested by the applicant.

An original and five copies of the completed and signed application must be submitted to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

## REVIEW CONSIDERATIONS

Review procedures of SDA applications will be the customary system of dual review: evaluation for scientific and technical merit by an initial review group of the appropriate funding component consisting primarily of nongovernment scientific experts, followed by evaluation for policy and program relevance by the appropriate National Advisory Council. Only applications recommended for approval by the Council will be considered for funding. Applications will be reviewed for the candidate's potential to develop into a productive alcohol, drug abuse, and/or mental health researcher. Reviewers will consider: (1) the qualifications of the candidate including the suitability of the candidate relative to the eligibility criteria and purposes of the SDA; (2) the soundness of the proposed career development plan; (3) the preceptor and institutional environment, including the institution's commitment to the candidate's career; (4) the nature and scientific/technical merit of the research plan; and (5) the appropriateness of the budget. Detailed review criteria are listed in the full PA.

## AWARD CRITERIA

The responsibility for award decision resides solely with authorized program staff of the funding component. The following criteria will be used in making award decisions: (1) overall merit of the proposal; (2) relevance of the proposal to the research priorities of the awarding Institute and program balance; and (3) availability of funds.

## INQUIRIES

The full PA, which includes the Special Instructions for preparing an SDA application, up-to-date policy guidelines, and the application forms may be obtained from any of the following offices:

National Institute on Alcohol Abuse and Alcoholism  
OSAP National Clearinghouse for Alcohol and Drug Information  
P.O. Box 2345  
Rockville, MD 20847-2345  
Telephone: (301) 468-2600 or 1-(800)-729-6686

National Institute on Drug Abuse  
Grants Management Branch  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

National Institute of Mental Health  
Grants Awards and Operations Section  
Grants Management Branch  
5600 Fishers Lane, Room 7C-05  
Rockville, MD 20857  
Telephone: (301) 443-4414

Inquiries regarding grants management may be directed to the NIMH address given immediately above.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.271, 93.277, 93.281. Awards will be made under the authority of Section 301 of the Public Health Service Act, as amended (42 U.S.C. 241) and administered in accordance with the PHS grants policy statement revised October 1990. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or health Systems Agency review.

#### INTEGRATED ADVANCED INFORMATION MANAGEMENT SYSTEMS

NIH GUIDE, Volume 21, Number 29, August 14, 1992

PA NUMBER: PA-92-100

P.T. 34; K.W. 1004017

National Library of Medicine

#### PURPOSE

The National Library of Medicine (NLM) wishes to provide planning and implementation grants to health science institutions that seek assistance in integrating their existing scattered databases and information systems into a comprehensive networked institutional information management system capable of serving clinical, research, educational, and administrative needs.

The Integrated Advanced Information Management Systems (IAIMS) program described in this Program Announcement (PA) is a substantially revised version of the NLMs existing IAIMS program, first announced in 1982.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Integrated Advanced Information Management Systems, is related to the priority area of surveillance and data systems. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applicants may be hospitals and medical centers, academic health science centers, and other appropriate health science organizations. Institutions that have received funding for Phase III "old" IAIMS projects may apply for other grant programs of the NLM, but are not eligible for "new" IAIMS support. All others, including those that have applied for IAIMS funding in the past, may apply to the revised program.

#### MECHANISM OF SUPPORT

The mechanism of support for this PA is the medical library resource grant (G08). This grant mechanism only funds direct costs.

#### PROGRAM OBJECTIVES

##### Background

In 1983 the NLM initiated an award program to provide "assistance to medical centers and health science institutions for planning and development projects leading to the implementation of Integrated Academic Information Management Systems (IAIMS)." The program announcement went on to say, "IAIMS are institution-wide computer networks that link and relate library systems with individual and institutional databases and information files, within and external to the institution, for patient care, research, education, and administration. The goal is to create an organizational mechanism within health institutions to more effectively manage the knowledge of medicine, and to provide for a system of comprehensive information access."

During the next decade over seventy institutions applied for IAIMS grants in one or another of the 3 defined phases, and through FY 1991 26 awards had been made to 16 institutions. The importance of information management today is as great as ever, but the program elements as originally defined by NLM deserve re-evaluation. Lessons have been learned from a decade of experience; furthermore, the climate has changed significantly as a number of institutions made extensive investments in information systems in recent years; most importantly, the advent of the High Performance Computing and Communications Initiative (HPCC) has

dramatically enriched the possibilities of information transfer, while increasing the complexity of information management.

The NLM is the lead biomedical organization in the federal Government's HPCC initiative. The HPCC program recognizes "that unprecedented computational power and its creative use are needed to investigate and understand a wide range of scientific and engineering 'grand challenge' problems." (1) Some of the problems identified are of obvious interest to biomedicine: National Research and Education Network (NREN), biotechnology, transmission of digital images, intelligent gateways to retrieve information from several life sciences databases, and innovations in educational techniques, among others.

Accordingly, NLM is revising its IAIMS program with:

- o A name change: replacing "academic" with "advanced" recognizes the wide applicability of the IAIMS concept and the need to incorporate new technology
- o Fusion of the old phases II and III (model and implementation) into one operational phase
- o Changes in the level of support
- o Some modification of the scope and conditions of the grant
- o Incorporation of HPCC into the NLM vision of an integrated information management system.

#### The Integrated Advanced Information Management Systems (IAIMS) Program

The revised IAIMS program has two phases: A planning phase, and an operational phase.

##### 1. IAIMS Planning Phase

"New" IAIMS planning phase resembles Phase I of the "old" IAIMS. Various models can be used in information systems planning, but all applications should include some form of self-study and allow for certain key elements:

- o A description of the institution's information management resources, current and five-year projection;
- o Development of an institutional information policy that addresses both short-term and long-term goals;
- o Identification of leadership for planning;
- o Broad involvement of clinical and basic science faculty, administration, and students;
- o Specification of desired strategic outcomes;
- o An outline of the planning process, including goals and timetables; and
- o A comprehensive view that considers information needs of patient care, research, education, and administration.

The outcome of planning activities is the development of an institutional Information Management Plan, which should include information resources management policies, an analysis of functions and responsibilities of major information database managers, and a description of how IAIMS will be developed, organized, and managed.

A total separation between planning and operations is not mandated; institutions vary widely in the information system already in place at the time of application. An institution may, if it wishes, use or introduce some operational elements during this planning period (for example, an E-mail system.)

The IAIMS planning grant may be for up to \$150,000 per year for one to two years. The grant supports direct costs only; funds are not provided for indirect or overhead costs.

##### 2. IAIMS Operational Phase

Health science institutions that complete the IAIMS planning phase successfully (or can demonstrate a comparably sophisticated information management plan based on their own planning efforts) may apply to NLM for an IAIMS operational phase grant to assist them in implementing the plan. Plans will vary for different institutions, but certain key elements are of interest to all:

###### A. Essential

- o A plan for developing the institution's information management resources, and the requisite networks;
- o A functional Information Management Policy;
- o Designation of leadership with appropriate background and status;
- o A plan for supporting IAIMS after termination of the grant;
- o Timetables for reaching key features of the operational plan;
- o Reasonable timetables for major plan features such as development of the network, organization of the management structure, appointment of the leadership, and post-grant financing plans. The ability of funded institutions to reach such milestones in a timely manner will be evaluated by the NLM when deciding annually on continuance of funding;
- o The ability to provide efficiently bibliographic and related literature pertinent to health care delivery and research. Significant participation by the health sciences library is essential; and
- o Substantial incorporation of one or more elements of HPCC/NREN into the institution's information system. Connection to Internet, for example, is one such element; other examples include collaboration through high speed networks, distance learning, addressing of computationally intensive problems in molecular biology in a distributed environment, visualization techniques, and network-based digital imaging.

###### B. Highly Recommended

- o A clear relationship to clinical aspects of the health sciences, such as linkage with a computerized patient record, a hospital information system, clinical alert information/distribution systems, clinically relevant expert systems, and/or systems for monitoring quality of care and cost-control; and

o Incorporation of current NLM objectives such as, connection to national networks, direct access to Medline and/or extensive use of Grateful Med, outreach components which improve information access for health care workers in underserved rural or inner city locations, and in other health care sites affiliated with the applicant.

#### C. Optional

o An apprenticeship in IAIMS may be incorporated into the operational plan at the discretion of the applicant, through a position entitled IAIMS Assistant. An educational program should be described, outlining the credentials of the candidates, the goals and duration of the apprenticeship, the structure of the learning experience, and other relevant material. Personnel, travel and supply costs may be requested up to a total of \$50,000 for each year of the operational phase. Costs for apprentices should be budgeted in accordance with standard institutional policy.

#### Other Information About the Operational Grant

The operational phase grant application may include an initial period of model development at the discretion of the institution, but a distinct interim period of model-building is not required.

Operational phase grants may be for up to \$500,000 per year for five years, or for up to \$550,000 per year for five years if support for the apprenticeship program is included. Only direct costs are supported.

NLM support for IAIMS at an institution will terminate at the end of the five-year operational phase, and is not renewable.

The word "institution" as used in this program description implies that IAIMS will involve all major organizational components of the institution to the extent feasible. The NLM realizes that large differences among medical centers are inevitable, and that at some sites, certain suborganizations may not be suitable for incorporation into the initial IAIMS plan. However, a plan that is restricted to a relatively small fraction of the institution has misunderstood the point of the program, and will not be favorably reviewed.

#### APPLICATION PROCEDURES

Applicants are to use the PHS 398 (rev.9/91) application form, that includes forms, instructions and additional information, available at most academic medical centers, the Extramural Programs office, NLM, at the address listed under INQUIRIES, and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/ 496-7441. Applications must be received by the standard NIH deadlines, October 1, February 1, and June 1. Late submissions will be held over for the subsequent review cycle. The title and number of this announcement must be typed in item 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 2450  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by the NLM Biomedical Library Review Committee, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the application will receive a second-level review by the NLM Board of Regents.

#### Critical Review Elements

##### For Planning Phase:

- o Responsiveness to the program description and guidelines;
- o Institutional environment;
- o Extent of involvement by key leadership; and
- o Short and long-term goals.

##### For Operational Phase:

- o Responsiveness to the program description and guidelines;
- o Institutional commitment to the IAIMS concept, including evidence of significant cost-sharing;
- o Plans for support of IAIMS after the granting period; and
- o Sophistication and feasibility of the operational plan.

#### AWARD CRITERIA

Applications will compete for available funding with all other applications assigned to the NLM. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review;
- o Availability of funds; and
- o Program balance considerations.



## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Mr. Richard T. West  
Extramural Programs  
National Library of Medicine  
Bethesda, MD 20894  
Telephone: (301) 496-3113  
FAX: (301) 402-0421

Direct inquiries regarding fiscal matters to:

Ms. Ellen G. Meltzer  
Extramural Programs  
National Library of Medicine  
Bethesda, MD 20894  
Telephone: (301) 496-4253  
FAX: (301) 402-0421

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.879. Awards are made under authorization of the PHS Act, Title III, Part A, Section 301, Title IV, Part D, Subpart 2, Sections 472-476, as amended, Public Law 100-607. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## REFERENCE

(1) Grand Challenges 1993: High Performance Computing and Communications

To obtain a copy of this report, which was prepared for the President's Office of Science and Technology Policy, call the IAIMS Program Officer (see above) or send request to: Federal Coordinating Council for Science, Engineering, and Technology Committee on Physical, Mathematical, and Engineering Sciences c/o National Science Foundation Computer and Information Science and Engineering Directorate 1800 G St., NW, Washington, DC 20550.

## ERRATA

### BIOTECHNOLOGY TRANSFER TO EPIDEMIOLOGIC STUDIES IN CANCER

NIH GUIDE, Volume 21, Number 29, August 14, 1992

RFA: CA/ES-92-23

P.T. 34; K.W. 0715035, 0760003, 785055, 0411005

National Cancer Institute  
National Institute of Environmental Health Sciences

Letter of Intent Receipt Date: October 22, 1992  
Application Receipt Date: November 19, 1992

This erratum is to correct the section MECHANISM OF SUPPORT in the Request for Applications (RFA) that was distributed via the E-Guide, Vol. 21, No. 27, July 31, 1992. The following is the corrected section in its entirety:

### MECHANISM OF SUPPORT

This program will be supported by traditional research project (R01) grants and Interactive Research Project Grants (IRPG). Awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

This RFA is a one-time solicitation. The total project period for applications submitted in response to the present RFA may not exceed three years. responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Competitive continuation applications will compete with all other unsolicited applications and be reviewed by standing Division of Research Grants study sections. If the NCI and NIEHS determine that there is a sufficient continuing program need, a request for renewal applications may be announced.

RFA: CA-92-21

P.T. 34; K.W. 0715035, 0785055, 1010013

National Cancer Institute

Letter of Intent Receipt Date: September 30, 1992

Application Receipt Date: November 12, 1992

This erratum is to correct the following sections of the Request for Applications (RFA) that was distributed via the E-Guide, Vol. 21, No. 27, July 31, 1992. The corrected sections are as follows:

#### MECHANISM OF SUPPORT

This program will be supported through National Institutes of Health (NIH) traditional research project grants (R01). responsibility for the planning, direction, and execution of the proposed research will be solely that of the applicant. Awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. (OASH) 82-50,000 revised October 1, 1990.

The RFA is a one-time solicitation. The total project period for applications submitted in response to the present RFA may not exceed three years. Competitive continuation applications will compete with all other unsolicited applications and be reviewed by Division of Research Grants (DRG) study sections. If the NCI determines that there is a sufficient continuing program need, the NCI may announce a request for renewal applications.

#### RESEARCH OBJECTIVES

##### Background

A decade or two ago, a biometry textbook, a medical statistics book, and an understanding of the basic principles of statistics provided applied biostatisticians with sufficient experimental designs and methodologic techniques to analyze most problems encountered in cancer research. Meanwhile, theoretical statisticians explored statistical problems of general interest without focussing on specific applications. Advances in biotechnology and high-speed computing tools have driven the development of specialties and even subspecialties in biostatistics. Advances have been made in methods for analyzing cancer survival data, understanding data with missing elements, allowing for errors in variables, fitting random effects models, and utilizing the bootstrap and other computationally intensive technologies. Most of this material is available only in technical journals and specialized textbooks on theoretical statistics

#### REVIEW CONSIDERATIONS

The first bullet under the review criteria should read:

- o extent to which application addresses research objectives of the RFA;

#### AWARD CRITERIA

The earliest anticipated date of award is July 1, 1993.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816



# NIH GUIDE

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## For Grants and Contracts

LIBRARY

AUG 25 1992

National Institutes of Health

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National Institutes of Health Room B4BN23,  
Building 31, Bethesda, Maryland 20892

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 30  
August 21, 1992

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

NOTICES

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES

ENVIRONMENTAL HEALTH SCIENCES CORE CENTER GRANTS PROGRAM

NIH GUIDE, Volume 21, Number 30, August 21, 1992

P.T. 34, 04; K.W. 0725005, 0710030, 0730070

National Institute of Environmental Health Sciences

This NOTICE is of a change of receipt date for this program to February 1 of each year.

The National Institute of Environmental Health Sciences (NIEHS) uses a variety of award mechanisms to accomplish its mission of studying the mechanisms and effects of environmental agents on human health. Among these are Environmental Health Sciences (EHS) Center Grants, a program of core center support (P30). The objective of this program is to provide core support for an administrative structure, scientific leadership, and shared core equipment to groups of productive scientists with programs in environmental health. The award allows these scientists to: (1) focus research efforts on issues of relevance to the NIEHS, (2) work in an environment conducive to inter-disciplinary approaches to such research; (3) serve as a resource to the NIEHS in providing scientific expertise on critical public health issues, and (4) engage in community outreach and education programs dealing with regional environmental health issues. A program of smaller Marine and Freshwater



Biomedical Sciences (MFBS) core center grants is also supported focusing on the use of aquatic species as biological models for environmental health research. Direct research support is NOT provided by the grant, except for limited funds for pilot projects and exploratory research.

The NIEHS currently supports 13 EHS centers and 5 MFBS centers. The funding of additional centers is subject to budgetary and other limitations. Because of these limitations and the special nature of the program, it is imperative that potential applicants contact NIEHS staff to discuss the scope, content, size, and timing of any applications for this program. In 1993, two extant EHS and one MFBS center will be competing for funding.

#### INQUIRIES

Guidelines for this program, including fiscal limitations, review criteria, and additional information are available from:

Dr. Christopher O. Schonwalder  
Chief, Scientific Programs Branch  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
104 Alexander Drive  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7634

#### RECEIPT DATES FOR NIEHS PROGRAM PROJECT (P01) APPLICATIONS

NIH GUIDE, Volume 21, Number 30, August 21, 1992

P.T. 34, 04; K.W. 0725005, 0710030, 0730070

National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences (NIEHS) announces a change in receipt dates for program project (P01) applications. Due to the newly announced receipt date for NIEHS core center (P30) applications of February 1, (see Notice in this issue titled: Environmental Health Sciences Core Center Grants Program), program project applications will not be received on this date. Therefore, submissions will be accepted only for the annual June 1 and October 1 receipt dates.

#### INQUIRIES

It is important that planned submissions be discussed with NIEHS program staff as content, focus, and size of these applications are critical factors in determining funding of these applications.

Inquiries about program project applications are to be directed to:

Dr. Thorsten Fjellstedt  
Deputy Director, Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
P.O. Box 12233  
Research Triangle Park, NC 27709  
Telephone: (919) 541-0131

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### INTERVENTIONS TO ENHANCE ADJUSTMENT TO CANCER RISK OR DIAGNOSIS

NIH GUIDE, Volume 21, Number 30, August 21, 1992

P.T. 34; K.W. 0414014, 0715035, 0745020, 0411005

RFA AVAILABLE: CA/NR-92-26

National Cancer Institute  
National Center for Nursing Research

Letter of Intent Receipt Date: September 18, 1992  
Application Receipt Date: December 8, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Cancer Institute (NCI) and the National Center for Nursing Research (NCNR) invite investigator-initiated grant applications for psychosocial research directed at improving the quality of life and increasing compliance with treatment regimen of cancer patients or adherence to early detection practices of persons at high risk of cancer.

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Interventions to Enhance Adjustment to Cancer Risk or Diagnosis, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone 202-783-3238.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local Governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). The applicant has sole responsibility for planning, direction, and execution of the proposed project. Total project period for applications submitted in response to this RFA may not exceed four years.

This RFA is a one-time solicitation. Future unsolicited competitive continuation applications will compete with all other investigator-initiated research grant applications and be reviewed according to the customary NIH peer review procedures.

#### FUNDS AVAILABLE

Total costs of \$2,400,000 per year for four years will be committed to specifically fund applications submitted in response to this RFA. It is anticipated that five to six awards will be made. This funding level is dependent upon the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI and the NCNR, the awards pursuant to this RFA are also contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

This RFA invites research to evaluate the impact of specific psychosocial counseling interventions in persons notified of increased cancer risk or newly diagnosed cancer patients with good prognosis. Objectives are: (1) to evaluate the efficacy of specific counseling interventions in high-risk individuals and newly diagnosed cancer patients, (2) to identify characteristics of successful interventions, and (3) to assess the potential for community implementation.

Counseling is short-term, time-limited therapy addressing emotional and adjustment issues of coping with risk or diagnosis of cancer, and issues such as the need to comply with early detection guidelines or initial treatment plans and medical follow-up. Interventions may include self-help or mutual support groups, behavioral interventions, individual counseling programs, and pharmacologic adjunctive therapy. Applications may incorporate existing but previously untested interventions, adapt existing programs for specific patient groups, or develop new interventions. Outcome variables must include quality of life and adherence/compliance with medical recommendations.

Interventions must target either (1) persons notified of increased risk of cancers for which primary prevention methods are not proven, but for which early detection is effective; or (2) newly diagnosed cancer patients with reasonable chance of cure or prolonged survival with state-of-the-art therapy. Investigators must also evaluate the program characteristics that contribute to efficacy and potential for transfer of the intervention into the community setting. A multi-disciplinary approach is recommended.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without documentation will not be accepted for review.

#### LETTER OF INTENT

Each prospective applicant is asked to submit, by September 18, 1992 a letter of intent that includes a descriptive title of the proposed research, the name, address, telephone/FAX numbers of the Principal Investigator, the names of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, it contains information that is helpful in planning for the review. It allows NCI and NCNR staff to estimate the potential review workload and to avoid conflict of interest in the review. The letter of intent is to be sent to the Program Director named in INQUIRIES.

## APPLICATION PROCEDURES

Applications must be received by close of business December 8, 1992. Application forms (PHS 398 (rev. 9/91)) and information about application procedures may be obtained from the NCI Program Director named in INQUIRIES.

## REVIEW CONSIDERATIONS

Applications that are competitive and responsive to the RFA will be evaluated scientific and technical merit by an appropriate peer review group according to specific review criteria. A second level of review will consider special needs and research priorities of NCI and NCNR.

## INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome. Direct requests for the RFA and inquiries regarding programmatic issues to:

Susan G. Wayfield, M.D., M.Sc.  
National Cancer Institute  
Executive Plaza North, Suite 300  
Bethesda, MD 20892  
Telephone: (301) 496-8541

Directed inquiries regarding fiscal matters to:

Mrs. Eileen M. Natoli  
National Cancer Institute  
Executive Plaza South, Suite 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.399, Cancer Control Research and 93.361, Nursing Research. Awards are made under the authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## THE EFFECTS OF SILICONE ON THE IMMUNE RESPONSE

NIH GUIDE, Volume 21, Number 30, August 21, 1992

RFA AVAILABLE: AI-92-11

P.T. 34; K.W. 0710070, 0740070, 0715015

National Institute of Allergy and Infectious Diseases  
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: September 15, 1992  
Application Receipt Date: November 20, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACTS NAMED IN INQUIRIES BELOW.

## PURPOSE

The Division of Allergy, Immunology and Transplantation (DAIT) of the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invite applications for studies focused on the short- and long-term effects of silicone polymers and their breakdown products on the cellular and molecular components of the immune system and its functions and how these changes might contribute to the initiation of self-reactivity and the induction of autoimmune disease.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, The Effects of Silicone on the Immune Response, is related to the priority area of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-782-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by public and private, foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply. Foreign institutions are not eligible to apply for the First Independent Research Support and Transition (FIRST) Award.

## MECHANISMS OF SUPPORT

The mechanisms of support for this program will be the research project grant (R01) and the FIRST Award (R29). The regulations (CFR Title 42, Part 52 and, as applicable to State and local governments, Title 45, Part 74) and policies that govern the research grant programs of the National Institutes of Health will prevail. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period may not exceed five years. The earliest anticipated award date will be July 1, 1993.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary NIH peer review procedures.

## FUNDS AVAILABLE

Up to \$650,000 total costs for the first-year, and additional approved expenses for up to five years, has been committed to fund applications submitted in response to this RFA. The NIAID and the NIAMS plan to make approximately three and one awards, respectively, in FY 1993, contingent on the receipt of highly meritorious applications. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and the availability of funds.

## RESEARCH OBJECTIVES

Silicone-containing implants and silicone injections have been linked to the development of autoimmune-like diseases, such as scleroderma, arthritis, and dermatomyositis, in some patients. However, there are no solid scientific data to support or rule out the link between the onset of autoimmune disease and the presence of silicone in intact and leaky implants. Furthermore, very limited information is available regarding the effects of silicone administration on the development of normal immune responses and the maintenance of self-tolerance. From the available preliminary information, it appears that some silicone polymers (e.g., D4) have biological activity in vivo similar to Freund's complete adjuvant. Basic research on the effects of silicone in the immune system will be valuable in determining the safety of these devices.

Examples of relevant research topics include, but are not limited to:

- o Effects of short- and long-term administration of silicone on the production, structure, and function of lymphocytes
- o Effects of intracellular accumulation of silicone and low molecular weight derivatives in macrophage function, including antigen processing and presentation, cytokine production, and cytotoxic activities.
- o Characterization of the profiles and fine specificity of autoantibodies obtained from the sera of patients developing autoimmune-like syndromes who have also received implants
- o Evaluation of the effects of silicone on lymphocyte and monocyte interactions with endothelial cells and fibroblasts and the production and function of adhesion molecules.
- o Analysis of silicone effects on the evolution of autoimmune disease in experimental systems, with regard to disease induction, course, and immunologic parameters

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are excluded or inadequately represented in clinical research, a specific justification must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit by September 15, 1992, a letter of intent that includes a descriptive title of the overall proposed research, the name and institution of the Principal Investigator, and a list of the names of key investigators and their institution(s). The letter of intent is requested in order to provide an indication of the number and scope of applications to be reviewed to allow early preparations for review. The letter of intent is not binding and does not commit the sender to submit an application, nor is it a requirement for submission of an application. The letter of intent is to be directed to:



Susana A. Serrate-Sztejn, M.D.  
Chief, Autoimmunity Section  
Clinical Immunology Branch  
Division of Allergy, Immunology and Transplantation  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4A20  
Bethesda, MD 20892  
Telephone: (301) 496-7985  
FAX: (301) 402-2571

#### APPLICATION PROCEDURES

Applications are to be submitted on the research project grant application form PHS 398 (rev. 9/91). These application forms are available in most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

The application receipt date is November 20, 1992.

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by an appropriate scientific peer review group convened by the Division of Research Grants, NIH. The second level of review will be provided by the National Advisory Allergy and Infectious Disease Council or the National Arthritis and Musculoskeletal and Skin Diseases Council in May 1993.

#### INQUIRIES

It is essential that prospective applicants obtain the full RFA prior to developing applications.

Direct inquiries regarding this program and requests for the RFA document to:

Susana A. Serrate-Sztejn, M.D.  
Chief, Autoimmunity Section  
Clinical Immunology Branch  
Division of Allergy, Immunology and Transplantation  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4A20  
Bethesda, MD 20892  
Telephone: (301) 496-7985  
FAX: (301) 402-2571

Dr. Michael D. Lockshin  
Director, Extramural Programs  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Building 31, Room 4C31  
Bethesda, MD 20892  
Telephone: (301) 496-0802

Direct inquiries regarding fiscal and administrative matters to:

Mr. Jeffrey Carow  
Chief, Immunology Grants Management Section  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B29  
Bethesda, MD 20892  
Telephone: (301) 496-7075

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.855 - Allergy, Immunology and Transplantation Research and No. 93.846 - Arthritis and Musculoskeletal and Skin Diseases Research. Grants are awarded under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## INTERACTIVE R01S FOR CLINICAL STUDIES OF SYSTEMIC THERAPIES

NIH GUIDE, Volume 21, Number 30, August 21, 1992

RFA AVAILABLE: CA-92-25

P.T. 34; K.W. 0715035, 0785035, 0745070

National Cancer Institute

Letter of Intent Receipt Date: October 22, 1992

Application Receipt Date: December 22, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

### PURPOSE

The Cancer Therapy Evaluation Program, Division of Cancer Treatment, at the National Cancer Institute (NCI) invites Interactive Research Project Grant (IRPG) applications (R01s) to perform research projects designed to conduct clinical studies of innovative systemic therapies investigating promising therapeutic approaches in a single tumor type or focused on a single class of novel compounds or a mechanism of action.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Interactive R01s for Clinical Studies of Systemic Therapies, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

### ELIGIBILITY REQUIREMENTS

Domestic and foreign, for-profit and non-profit organizations, governments and their agencies are eligible to apply. Applications may be from single institutions or multiple institutions (collaborating institutions, consortia, cooperative groups). New and experienced investigators are encouraged to apply. Applications from minority individuals and women are encouraged. Applicants proposing to perform phase I clinical trials that address issues on the mechanisms of action of immunologically active agents are not eligible for this RFA and should apply for an RFA that will be issued by the Biological Response Modifiers Program in the near future.

### MECHANISM OF SUPPORT

Support of this program will be through the IRPG, an assistance mechanism composed of three or more investigator-initiated research grant applications (R01s) that will be reviewed independently for merit, but that share a theme and resource(s) and require concurrent funding to maximize the effectiveness of the resource or to allow maximal creative interaction between researchers. Except as otherwise stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

This RFA is a one-time solicitation for FY 93. However, the NCI has plans to re-issue this RFA for funding in 1994. If it is determined that there is a sufficient continuing program need, the NCI will invite recipients of awards under this RFA to submit competitive continuation applications for review according to the procedures described below.

### FUNDS AVAILABLE

Approximately \$4,000,000 in total costs per year for four years will be committed to fund applications submitted in response to this RFA. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The total cost for each IRPG (consisting of three or more R01s) is limited to \$750,000 per year. Thus it is anticipated that five to six IRPGs will be funded in FY 93. In FY 93, it is anticipated that this RFA will be re-advertised and an additional three IRPGs will be funded in FY 94. The total project period for applications submitted in response to the RFA may not exceed four years. The earliest feasible start date for the initial awards will be August 1993. Although this program is provided for in the financial plans of the NCI, the award of R01 grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

### RESEARCH OBJECTIVES

#### Background

An unprecedented number of new therapeutic agents are ready for evaluation in pilot clinical studies. In addition, insights into the biologic function and clinical relevance of growth factors, genes that promote and suppress neoplasia, mechanisms of treatment sensitivity and resistance, and function of the immune system provide important new clinical research opportunities for investigators. The NCI is interested in expanding support for clinical research. Under this IRPG RFA, the NCI encourages the coordinated submission of related

research project grant applications from investigators who want to collaborate on a common cancer research theme, but do not require extensive shared physical resources or core functions. This mechanism is not meant to replace the program project (P01) mechanism but to support a level of collaboration between that of the P01 and that available through an individual R01.

#### Research Goals And Scope

The aims of this RFA are two-fold: (1) to provide support for translational research that brings innovative basic research findings into the clinic and (2) to foster the development of interactions between basic science laboratories of different disciplines and clinicians performing clinical trials to advance therapeutic clinical research.

This RFA is soliciting applications to perform interactive research projects with the goal of developing new clinical studies involving systemic therapies with a therapeutic intent. The IRPGs may have as their key focus either: (1) clinical studies investigating promising therapeutic approaches in a single tumor type or (2) the development of new clinical treatment strategies focused on a single class of novel compounds or mechanism of action. Each project supported in the IRPG is expected to contribute to and be directly related to the common theme of the IRPG application. The application must clearly explain how the projected integrated R01 research grants can be expected to accomplish the stated goal more efficiently and effectively than they could without the anticipated interactions. At least one clinical trial protocol must be proposed in one of the grant applications. The clinical trials should be well integrated with the laboratory studies proposed within the same R01 application or in separate R01 applications.

#### SPECIAL REQUIREMENTS

The RFA describes the roles and responsibilities of the Principal Investigator/Awardee and the Project Coordinator.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF FEMALES AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of females and minorities in study populations. If females or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by October 22, 1992, a letter of intent that includes a descriptive title of the proposed research, the names and addresses of the Principal Investigator, the names of other investigators and key personnel, the participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, it is requested in order to provide an indication of the number and scope of applications to be reviewed.

The letter of intent is to be sent to Dr. Roy S. Wu at the address under INQUIRIES.

#### APPLICATION PROCEDURES

Applications must be received by December 22, 1992. If an application is received after that date, it will be returned to the applicant without review. The PHS 398 (rev. 9/91) research grant application form is to be used in applying for this RFA. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441; and from the NCI Program Directors named below.

A short narrative of the interactive nature of the research applications should be included in the Research Plan of each of the R01 applications. The exact nature of the interactions should be clearly detailed under the consortium section of the respective R01 applications.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the program requirements and criteria stated in the RFA is an NCI program staff function. Applications that are judged non-responsive will be returned to the applicant. Questions concerning the responsiveness of proposed research to the RFA are to be directed to Program Directors (see INQUIRIES).

#### AWARD CRITERIA

The anticipated date of award is August 1, 1993. In addition to the technical merit of the application, the NCI will consider how well the applicant institution meets the goals and objectives of the program as described in the RFA, availability of resources, and study populations.

## INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA, inquiries about whether or not specific proposed research would be responsive, and requests for the RFA are encouraged and are to be directed to NCI Program Directors at the addresses below. The NCI Program Directors welcome the opportunity to clarify any issues or questions from potential applicants.

For technical information:

Dr. Roy S. Wu  
Ms. Diane Bronzert  
NCI Program Director  
Cancer Therapy Evaluation Program  
Division of Cancer Treatment  
National Cancer Institute  
Executive Plaza North, Room 734  
Bethesda, MD 20892  
Telephone: (301) 496-8866  
FAX: (301) 480-4663

For business information:

Ms. Sara Stone  
Grants Management Specialist  
National Cancer Institute  
Executive Plaza South, Room 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800, ext. 66  
FAX: (301) 496-8601

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No 93.395, Cancer Treatment Research. Awards are made under the authorization of the Public Health Service Act, Title IV Sections 301, 410, and 411, Part A (Public Law 78-410, 42 USC 241 as amended, Public Law 99-158, 42 USC 285a) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ONGOING PROGRAM ANNOUNCEMENTS

### RESEARCH ON ECONOMIC AND SOCIOECONOMIC ASPECTS OF ALCOHOL ABUSE

NIH GUIDE, Volume 21, Number 30, August 21, 1992

PA AVAILABLE: PA-92-101

P.T. 34; K.W. 0404003, 0408006, 0785055

National Institute on Alcohol Abuse and Alcoholism

THE PROGRAM ANNOUNCEMENT ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

Alcohol abuse and alcoholism are major problems in the United States, and costs related to alcohol misuse are a significant economic issue. The purpose of this Program Announcement (PA) is to make clear the continued interest of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in supporting additional, high-quality research on economic and socioeconomic aspects of the prevention, treatment, and epidemiology of alcohol-related problems.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas (DHHS, 1990(a)). This PA, Research on Economic and Socioeconomic Aspects of Alcohol Abuse, is related to the priority areas of decreasing morbidity and mortality that are associated with the drinking of alcohol. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0, or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign non-profit and for-profit organizations, whether public or private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and



eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply. Foreign institutions are not eligible to apply for the First Independent Research Support and Transition (FIRST) Award.

#### MECHANISMS OF SUPPORT

Research support may be requested through applications for a regular research grant (R01), Small Grant (R03), or FIRST Award (R29). Specialized announcements for the FIRST Award program (R29) and the Small Grant program (R03) are available from the National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20852, telephone (301) 468-2600 or 1-800-729-6686.

Applicants for R01s may request support for up to five years, Small Grants are limited to two years, and FIRST Award applicants must request five years of support. FIRST and Small Grants are not renewable, but applications may be submitted for R01 support to continue research on the same topics.

#### AVAILABILITY OF FUNDS

No specific set-aside funds are being allocated by the NIAAA for this program at this time. Applications received in response to this PA will compete with others assigned to the NIAAA for funding. The amount of funding available will depend on appropriated funds, quality of research applications and program priorities at the time of the award. In FY 1992, 29 grants relating to this program area, including new and continuation grants, were funded for approximately \$6 million.

#### RESEARCH OBJECTIVES

The purpose of this PA is to stimulate research applications in five areas of study: (1) the price and availability of alcoholic beverages; (2) advertising and media portrayals of alcoholic beverages; (3) risk-taking behavior and its relationship to drinking; (4) the deterrence of drinking and driving; and (5) the costs and financing of alcoholism treatment services.

#### Background

Economic considerations often have a strong direct or indirect effect on the levels of alcohol consumption and on the levels of alcohol-related problems. The price and availability of alcoholic beverages, for example, have been shown to affect alcohol consumption, morbidity, and mortality. Advertising by the alcohol industry supports a significant share of prime-time television, but the effects of advertising on alcohol use and abuse are still not clear. Public information campaigns, alone or in combination with more personalized approaches, may be used to prevent alcohol problems, but the cost-effectiveness of such intervention strategies should be more firmly established. Risk-taking behavior may be conceptualized in economic terms according to rational and quasi-rational models of decision-making. Costs, as well as other social policy considerations, affect the choice of strategies for deterring drinking and driving and the ways such interventions are implemented. The costs and methods of financing alcoholism treatment are also of interest in the PA.

#### Scope

Some examples of research topics that would be considered responsive to this announcement include the following:

- o the effects of price changes and availability controls on levels of alcohol consumption and alcohol-related problems
- o variations in price and income elasticities among different types of drinkers (heavy, moderate, light) or among demographic subgroups (e.g. youth)
- o the impact of changes in alcohol taxation on economic efficiency, equity, and the public health
- o the impact of advertising on the development of alcohol expectancies and drinking behavior, especially among youth
- o the effectiveness of health promotion messages
- o the development and testing of cost-benefit models of risk taking behavior, especially among youth
- o the effects of types, levels, and combinations of sanctions in producing both general and specific deterrence to drinking and driving
- o evaluations of non-sanction-based deterrence initiatives for drinking driving such as server intervention, designated driver campaigns, and the provision of alternative means of transportation
- o the costs and cost offsets of different modalities for the treatment of alcoholism
- o the relationships between treatment factors, patient characteristics, facility characteristics, and treatment costs
- o patterns of treatment utilization and treatment seeking characteristics

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS ON THE INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

### APPLICATION PROCEDURES

Applicants are to use the grant application form PHS 398 (rev. 9/91). The number and title of this program announcement, PA-92-101, Research on Economic and Socioeconomic Aspects of Alcohol Abuse, must be typed in item number 2a on the face page of the PHS 398 application form.

Application kits containing the necessary forms and instructions may be obtained from business offices or offices of sponsored research at most universities, colleges, medical schools, and other major research facilities. If such a source is not available, the following office may be contacted for the necessary application material:

National Clearinghouse for Alcohol and Drug Information  
P.O. Box 2345  
Rockville, MD 20852  
Telephone: (301) 468-2600

The signed original and five permanent, legible copies of the completed application must be submitted to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

### REVIEW CONSIDERATIONS

The Division of Research Grants, NIH, serves as the central point for receipt of applications for most discretionary PHS grant programs. Applications received under this announcement will be assigned to Initial Review Groups (IRGs) in accordance with established PHS Referral Guidelines. The IRG, consisting primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit. Notification of the review recommendations will be sent to the applicant after the initial review. Applications will receive a second-level review by an appropriate National Advisory Council, whose review may be based on policy considerations as well as scientific merit. Only applications recommended by the Council may be considered for funding.

### AWARD CRITERIA

Applications recommended by a National Advisory Council will be considered for funding on the basis of overall scientific and technical merit of the research as determined by peer review, program needs and balance, and availability of funds.

### INQUIRIES

Potential applicants are encouraged to seek preapplication consultation. They may contact any of the following for information on preparing an application.

Michael Hilton, Ph.D.  
Prevention Research Branch  
Division of Clinical and Prevention Research  
National Institute on Alcohol Abuse and Alcoholism  
5600 Fishers Lane, Room 13C-23  
Rockville, MD 20857  
Telephone: (301) 443-1677

Inquiries relating to fiscal matters are to be directed to:

Elsie Fleming  
Grants Management Branch  
Office of Planning and Resource Management  
National Institute on Alcohol Abuse and Alcoholism  
5600 Fishers Lane, Room 16-86  
Rockville, MD 20857  
Telephone: (301) 443-4703

### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.273. Awards are made under the authority of Sections 301 and 510 of the Public Health Service Act, as amended (42 USC 241 and 290bb). Federal

regulations at 42 CFR Part 52, "Grants for Research Projects," and Title 45 CFR Parts 74 and 92, generic requirements concerning the administration of grants, are applicable to these awards. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### RESEARCH ON SURVEILLANCE AND RELATED STUDIES OF SPORTS INJURY IN YOUTH

NIH GUIDE, Volume 21, Number 30, August 21, 1992

PA NUMBER: PA-92-102

P.T. 34; K.W. 0785205, 0715027, 0745030

National Institute of Arthritis and Musculoskeletal and Skin Diseases

#### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites grant applications to conduct surveillance and related research projects on sports injury in youth.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement, Research on Surveillance and Related Studies of Sports Injury in Youth, is related to the priority area of physical activity, fitness, and unintentional injuries. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, non-profit and for-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State and Local governments, and eligible agencies of the Federal Government. However, foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) Award (R29) and the career development awards (K04, K08, K11). Applications from minority individuals and women are encouraged.

#### MECHANISMS OF SUPPORT

Support will be offered through research project grants (R01), FIRST Awards (R29), research fellowship training awards (F32, F33), and research career development awards (K04, K08, K11).

#### RESEARCH OBJECTIVES

Sports and exercise activity in youth are critical to developing and maintaining physical fitness and general well-being. These fitness patterns established in youth may provide the basis for a healthy life-style throughout adult life. The occurrence of injuries has been accepted as a natural risk associated with exercise and especially with sports participation. Of the estimated 8 million youth participating in sports at the junior high and high school level, approximately 25 percent incurred some form of injury. Therefore, the physical and financial impact is significant.

One means of reducing these injuries is to understand the nature and risk factors for sports injuries and to seek preventive measures to reduce the occurrence. Injury surveillance approaches have led to important changes in rules and equipment to reduce the rate of injury. In one case, trampolines, the nature of the sport could not be modified to improve safety, therefore, the sport has been eliminated.

On April 8-9, 1991, at the Lister Hill Center of the NIH a conference was held on Sports Injuries in Youth: Surveillance Strategies. This meeting was co-sponsored by the National Advisory Board for Arthritis and Musculoskeletal and Skin Diseases, NIAMS, and the Centers for Disease Control. The purpose of the Conference was to examine the various factors required to develop and operate a surveillance system. Successful systems and problem areas were described. The resulting information will provide guidance for researchers entering areas of investigation involving development and utilization of reliable data bases in the field of scholastic sports injury. Published proceedings from the conference are available from the contact person listed below under INQUIRIES.

The epidemiologic definition of surveillance is the dynamic, close, and continued watchfulness over the distribution and trends of disease occurrence through systematic collection, tabulation, and analysis of relevant mortality and morbidity data. Essential steps in this process include data collection, entry, processing, analysis, interpretation, and presentation. A weakness in any of these procedures may result in incomplete, inaccurate, improper, or poorly disseminated findings. One of the critical elements in analyzing sports surveillance data is the determination of the rate (incidence/number of persons at risk) of injury. For example, all players on a basketball team may not be at equal risk, since some may not even enter the game. Issues such as these are well defined in the conference proceedings.

The suggested areas for future research that were developed during the conference were defined in the

proceedings as:

- o Developing surveillance systems for consistent national data collection;
- o Developing a national sports injury data base;
- o Injury characterization and intervention schemes;
- o Coordination of data from diverse sources;
- o Developing methods for "small area sampling" of special injury situations;
- o Evaluating re-injury rates and risks;
- o Expanding surveillance to include intramural and extra-scholastic sports;
- o Expanding injury surveillance to include primary grades;
- o Comparing injury rates and conditions to college and professional sports;
- o Considering a wide range of external factors that may add to risks; and
- o Developing and evaluating instructional prevention programs.

These areas of research are neither prioritized nor meant to be restrictive. Investigators are encouraged to submit applications in any meritorious area of research responsive to the general research objectives of this Program Announcement. In addition to projects that specifically address surveillance methodology to uncover risks of and the nature of injuries, the NIAMS will consider to be responsive to this announcement applications that include biomechanical, biochemical, or other approaches to elucidating the mechanism of injury. Such related studies should either (1) be a component of applications for surveillance-based research or (2) be based on the findings of other surveillance data indicating that a particular mechanism may be the cause of injury.

The project should be founded on a strong hypothesis as evidenced by preliminary data of the investigator or others. All data collection and statistical procedures should be fully defined and justified.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study. Special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in Form PHS 398 in Sections 1-4 of the Research Plan and then summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, and Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including, but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities. If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed and the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in the priority score assigned to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on grant application form PHS 398 (rev. 9/91), except for individual fellowship applications which must be submitted on form PHS 416-1 (rev. 10/91). Applications will be accepted at the standard application deadlines indicated in the application kits.



Application kits are available at most institutional business offices and may also be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in Section 2a on the face page of form PHS 398.

The completed original application and five legible copies of form PHS 398 or two copies of form PHS 416-1 must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications will be reviewed for scientific and technical merit by initial review groups of the Division of Research Grants, NIH, or by the review group of the appropriate Institute, Center, or Division (ICD), in accordance with the standard NIH peer review procedures. Following scientific-technical review, applications will receive a second-level review by the appropriate national advisory council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that ICD. The following criteria will be considered in the making of funding decisions:

- o Quality of the proposed project as determined by peer review;
- o Availability of funds; and
- o Program balance among research areas of the announcement.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Stephen L. Gordon, Ph.D.  
Chief, Musculoskeletal Diseases Branch  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 407  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 402-3338

Direct inquiries regarding fiscal matters to:

Ms. G. Carol Clearfield  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 726B  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 402-3360

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, (Arthritis, Musculoskeletal and Skin Disease Research). Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

RESEARCH SUPPLEMENTS TO PROMOTE REENTRY INTO BIOMEDICAL AND BEHAVIORAL RESEARCH CARE...

NIH GUIDE, Volume 21, Number 30, August 21, 1992

P.T. 34, 11; K.W. 0710030, 1014006

National Institutes of Health

This announcement that appeared in the NIH Guide for Grants and Contracts, Vol. 21, No. 25, July 10, 1992, contained an incorrect address for the National Institute of Allergy and Infectious Diseases. The following is the correct address:

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES:

Milton J. Hernandez, Ph.D.  
Director, OSTMD, DEA, NIAID  
Solar Building, Room 4C10  
Bethesda, MD 20892  
Telephone: (301) 496-7291

APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE SOLAR BUILDING IS:

6003 Executive Boulevard  
Rockville, MD 20852

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 31  
August 28, 1992

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIH-CU.*

# NOTICES

## WORKSHOP ON MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

NIH GUIDE, Volume 21, Number 31, August 28, 1992

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health (NIH), Office for Protection from Research Risks (OPRR), is continuing to sponsor workshops on implementing the Public Health Service Policy on the Humane Care and Use of Laboratory Animals. Each of the workshops scheduled for FY 1993 will focus on a specific theme.

The workshops are open to institutional administrators, members of Institutional Animal Care and Use Committees, laboratory animal veterinarians, investigators, and other institutional staff who have responsibility for high-quality management of sound institutional animal care and use programs.

Date: December 3-4, 1992

(Topic: MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS)

Workshop Site: Nashville, TN

Sponsors: Vanderbilt University and Meharry Medical College

## INQUIRIES

Ms. Marilyn Dasaro  
Division of Continuing Medical Education  
Vanderbilt University  
D-8211 Medical Center North  
Nashville, TN 37232-2337  
Telephone: (615) 822-4030  
FAX: (615) 343-0809



NATIONAL HUMAN SUBJECT PROTECTION WORKSHOPS

NIH GUIDE, Volume 21, Number 31, August 28, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The Office for Protection from Research Risks (OPRR) of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on the responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

**SOUTHWESTERN WORKSHOP**

**DATES:** November 16 & 17, 1992

**LOCATION:**

Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

**SPONSORS:**

University of Texas Health Science Center at Houston  
Prairie View A & M University

**REGISTRATION:**

Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

**TITLE:** Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

**DESCRIPTION:** Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems that this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, other health care professionals, clergy, lawyers, medical, nursing, social work students, and psychologists as well as IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

**SOUTHEASTERN WORKSHOP**

**DATES:** January 14 & 15, 1993

**LOCATION:**

Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

**SPONSORS:**

University of South Florida  
Florida A&M University

**REGISTRATION:**

Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FA0-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

**TITLE:** Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

**DESCRIPTION:** Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers often impact the pool of subjects that an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. IRB members, students in health care areas, and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests through question and answer sessions and informal discussions.

#### **SOUTHWESTERN WORKSHOP**

**DATES:** February 12 & 13, 1993

#### **LOCATION:**

Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

#### **SPONSORS:**

Arizona State University  
Northern Arizona University

#### **REGISTRATION:**

Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

**TITLE:** Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

**DESCRIPTION:** This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences, Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

#### **INQUIRIES**

For further information regarding these workshops or future NIH/FDA National Human Subject Protections Workshops, please contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

#### **PHS GRANTS AND CONTRACTS TRAINING COURSE**

**NIH GUIDE**, Volume 21, Number 31, August 28, 1992

P.T. 34; K.W. 1014002, 1014006

Public Health Service

**SUMMARY:** The Office of the Assistant Secretary for Health is announcing a training course entitled "Orientation to PHS Grants and Contracts Activities for Applicants and Recipients of Awards" which will be presented 12 times at locations around the country during FY 1993. Complete information as to locations and dates is provided below under SUPPLEMENTARY INFORMATION.

**DATES:** To receive consideration for a particular course session, applications must be received by the close of business on the deadline date specified under SUPPLEMENTARY INFORMATION below.

#### SUPPLEMENTARY INFORMATION:

COURSE TITLE: "Orientation to PHS Grants and Contracts Activities for Applicants and Recipients of Awards."  
NOTE: This is not a course on grant-writing. Rather, it is designed to provide a broad overview of how to conduct business with PHS using the grant and contract mechanisms.

COURSE DESCRIPTION: This is a two-day course that is designed to provide applicants for and recipients of PHS grants and contracts a better understanding of the procedures and expectations in applying for funding and administering an award from the PHS. Day one of the course concentrates on the grants process; day two is devoted to contracting. Students will be provided with a broad overview of conducting business with the PHS including how it is organized, when the grant or contract mechanism is used, how the PHS contracts and grants processes are structured, how to identify grant and contract funding opportunities, how to submit effective applications and proposals, and how to properly administer a contract or grant after it has been awarded.

TARGET POPULATION: Grant and contract staff of organizations that are presently doing business with the PHS or that plan to submit applications for grants or proposals for contracts. The course is intended for staff who are inexperienced with the grant and contract mechanisms.

DATES - 1992	LOCATIONS	APPLICATION DEADLINES
October 13-14	Winston-Salem, NC	September 10
November 9-10	Atlanta, GA	October 10
December 7-8	Rockville, MD	October 10

#### DATES - 1993

January 25-26	San Diego, CA	October 10
February 22-23	Kansas City, MO	January 10
March 17-18	Dallas, TX	January 10
April 19-20	San Francisco, CA	January 10
May 17-18	Seattle, WA	January 10
June 15-16	Rockville, MD	May 10
July 12-13	Boston, MA	May 10
August 16-17	Chicago, IL	May 10
September 20-21	Denver, CO	May 10

All courses will be held from 8:30 AM to 5:00 PM both days.

Selection will be made on a first-come, first-served basis.

Early application is encouraged because these offerings are filled rapidly.

#### COURSE OUTLINE:

##### DAY 1

Introduction to PHS Assistance (grants/cooperative agreements) and Acquisition (contracts): PHS Mission and Organizational Structure; Assistance vs. Acquisition (The Federal Grant and Cooperative Agreement Act); PHS Grant and Contract Expenditures and Recipients; Introduction to Types and Purposes of PHS Grants; Roles of PHS Grants and Program Management Staff.

Seeking and Applying for PHS Grants/Cooperative Agreements: Sources of Information; Understanding Program Announcements; The Application Package; The Complete, Effective Application; Competition and Objective Review.

Negotiation and Award Process for Grants/Cooperative Agreements: Cost Analysis and Preaward Review; Negotiating--Clarifying and Revising Proposed Activities; Funding Outcomes; Contents of a Grant Award Document; General and Special Conditions.

Grant/Cooperative Agreement Post-Award Issues and Concerns: Monitoring; Audit; Appeals; Progress Reports; Drawdowns; Financial Status Reports; Grant Budget Control; Cost Principles and Unallowable Costs; Purchasing; Property Management.

##### DAY 2

Seeking PHS Contracts: Identifying PHS Contracting Opportunities; The Legal Framework of PHS Contracting; Small Business Contracting Programs; Roles of PHS Contracting and Project Staff.

Responding to Contract Solicitations: Small Purchases - \$25,000 or Less; Purchases Greater Than \$25,000; Preparing the Technical Proposal; Preparing the Business Proposal.

Proposal Submission, Contract Negotiation, and Award: Proposal Submission and Evaluation; Negotiation and Award.

Contract Administration: Initial Contract Administration Steps; Significant Contract Administration Concerns.

CLASS SIZE: Limited to 30 participants per session to maximize interaction and only one individual per institution, per session.

ATTENDANCE: Those accepted will be expected to attend both full days of the course. A Certificate of Attendance will be issued to all participants who attend for both days.

COST: There will be no charge for this course. Travel and accommodations will be the responsibility of participants.

#### NOTIFICATION OF APPLICANTS:

Applicants selected will be notified of their acceptance approximately one month in advance of the course and provided with information on the exact training location and suggested accommodations. Persons not selected will not be notified.

TO APPLY: Submit to the Training Coordinator a letter on the employing organization's letterhead which provides all of the following information. Incomplete applications cannot be considered:

Name of applicant  
Employing organization: name, address, and telephone number  
Position title of applicant  
Years of experience with PHS grants, contracts, or both  
Principal area of interest (grants, contracts, or both)  
Reason for wanting to take this course (100 words or less)  
Course session desired

#### INQUIRIES

Letters of application and requests for information are to be sent to:

Training Coordinator  
Grants Policy Branch  
Division of Grants and Contracts  
Office of the Assistant Secretary for Health  
Parklawn Building, Room 17A-45  
5600 Fishers Lane  
Rockville, MD 20857

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

##### OBESITY PREVENTION IN AMERICAN INDIANS/ALASKA NATIVES: COORDINATING CENTER

NIH GUIDE, Volume 21, Number 31, August 28, 1992

RFA AVAILABLE: NIH-92-HL-09-P

P.T. 34; FE; K.W. 0715145, 0745027

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: October 15, 1992

Application Receipt Date: December 18, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Epidemiology and Clinical Applications (DECA) invites cooperative agreement applications for a Coordinating Center to participate [with an estimated five Field Centers, to be selected under a separate RFA: NIH-92-HL-08-P, and with the assistance of the National Heart, Lung, and Blood Institute (NHLBI)] in a collaborative study to assess the effectiveness of school-based intervention to prevent obesity in young American Indians/Alaska Natives (Native Americans). The solicitation is for the initial three-year planning and feasibility study of a planned nine-year effort.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. The RFA, Obesity Prevention in American Indians/Alaska Natives, is related to the priority areas of nutrition, physical activity fitness, educational and community-based programs, heart disease and stroke, and diabetes and chronic disabling diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Foreign organizations are not eligible to apply and domestic applications may not include international components. Applications from minority individuals, especially American Indians/Alaska Natives, and women are encouraged.



## MECHANISM OF SUPPORT

The administrative and funding mechanism to be used to undertake this project will be a cooperative agreement (U01), an assistance mechanism. Under the cooperative agreement, the NIH assists, supports, and/or stimulates and is involved substantially with recipients in conducting a study by facilitating performance of the effort in a "partner" role.

## FUNDS AVAILABLE

One award for the Coordinating Center will be made under the RFA. A maximum of \$6.3 million (including direct and indirect costs) over a three-year period will be awarded for Field Centers and the Coordinating Center with at least two-thirds for Field Centers. First year total funding will be \$2.0 million.

## RESEARCH OBJECTIVES

### Background

The Native American population, including American Indians and Alaska Natives, totals nearly 1.5 million from over 500 tribes and nearly 300 reservations and Alaska Native villages. Earlier in this century, heart disease was rarely noted in Native Americans but, in the last decade, cardiovascular disease has become the leading cause of death in Native Americans. Several factors may be responsible for this increase, one of which is an increasing incidence of obesity. Reduction of the prevalence of obesity in Native Americans has been designated as a goal for improving the health of this minority population. The RFA attempts to address these issues with a project on primary prevention of obesity in young Native Americans.

### Objectives and Scope

This study is envisioned as a nine-year effort to develop and test intervention to reduce the rate of weight gain in schoolchildren of the Native American community. The study consists of two phases. Feasibility of the concept will be determined during the first three years of the study (the subject of the RFA described by this announcement). If feasibility is demonstrated, the NHLBI anticipates inviting competitive continuations for implementing the full-scale study over the next six years. The planning and feasibility study (Phase I) may be loosely divided into three subphases covering about a three-year period.

Phase I(a): Planning and Protocol Development - 1 year.

Phase I(b): Training and Pilot-testing - 1 year and 6 months.

Phase I(c): Post-Pilot-testing Assessment - 6 months.

Possible objectives of Phase I(a) are to develop a complete study protocol, data forms, and a manual of operations, and to recruit and prepare for the work with the schools.

The main activities of Phase I(b) are envisioned to include training of intervention personnel, conducting the pilot test of the study protocol that was developed in Phase I(a), and evaluating and cooperatively revising the study materials and methods.

Phase I(c) is expected to include refinement of the protocol, intervention and measurement manuals and study materials as well as manuscript preparation. Analyses of the data will be completed. The goal of these analyses will be to evaluate acceptance and adherence to interventions and the effects of the interventions.

The planning and feasibility study is expected to be completed over approximately a three-year period. During this period, investigators from the Field Centers, Coordinating Center, and the NHLBI will collaboratively develop the study design, materials, forms, protocol, and manual of operations to be cooperatively followed by all Field Centers and Coordinating Center in the pilot test and subsequent full-scale study if it is approved. Some aspects of the protocol may vary by center to meet local conditions and needs. The expertise of the investigators will be fully utilized to collaboratively determine the most appropriate approach to prevent obesity among young Native Americans.

The objective of Phase II - not within the scope of the current awards, but relevant to the current RFA - will be to conduct a full-scale randomized intervention trial to prevent the development of obesity. It is envisioned that the intervention will be focussed on pre-adolescent elementary schoolchildren and that about 3000 Native American students study-wide will participate in intervention and control groups. Schools are expected to be the unit of randomization. An estimated six schools per center may be required in the full-scale study. The intervention is envisioned to last three to four years, depending on the time needed to show measurable difference in the selected obesity index between the intervention and control groups. (Note that this is not weight loss but a reduction in the rate of weight gain.) Data analysis and publication of study results will follow the completion of the intervention.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by October 15, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows the NHLBI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

C. James Scheirer, Ph.D.  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 548  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7363  
FAX: (301) 402-1660

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these awards. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441; and from the NIH Project Scientists named below.

Applications must be received by December 18, 1992. An application not received by this date will be considered ineligible.

#### REVIEW CONSIDERATIONS

Applicants are encouraged to submit and describe their own ideas on how best to meet the goals of the study, but they are expected to address issues identified under SPECIAL REQUIREMENTS of the Request for Applications. NOTE THAT THIS DOCUMENT IS NOT THE REQUEST FOR APPLICATIONS. Applications will be judged primarily on the scientific quality of the application, the discussion of considerations relevant to the RFA, expertise of the investigators, their capability to perform the work proposed, and a demonstrated willingness to work together with other Centers and the NHLBI Project Scientists.

The review group will assess (as further detailed in the RFA):

- o Scientific merit of the study.
- o Organizational and administrative ability to serve as a Coordinating Center for a multicenter randomized controlled intervention trial.
- o Qualifications, experience, and commitment of key personnel.
- o Facilities and equipment to function as a Coordinating Center for a multicenter intervention trial.
- o Appropriateness of the budget for the work proposed.

#### AWARD CRITERIA

Applications recommended by the National Heart, Lung, and Blood Advisory Council will be considered for award based upon (a) scientific and technical merit and the requirements explicitly stated in the RFA, (b) program balance, including in this instance, sufficient compatibility of features to make a successful collaborative program a reasonable likelihood, and (c) availability of funds.

#### Time Table

Letter of Intent:	October 15, 1992
Application Receipt Date:	December 18, 1992
Review by National Heart, Lung, and Blood Advisory Council:	May, 1993
Anticipated Award Date:	July 1, 1993

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Requests for a copy of the RFA and inquiries regarding this announcement may be directed to:

Richard R. Fabsitz  
Clinical and Genetic Epidemiology Branch  
Division of Epidemiology and Clinical Applications  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3A17  
7750 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-4333

Direct fiscal and administrative matters to:

Marie Willett  
Deputy Chief, Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A12  
Bethesda, MD 20892  
Telephone: (301) 496-7255

#### AUTHORITY AND REGULATIONS

This project is described in the Catalog of Federal Domestic Assistance No. 93.837. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR 74. This project is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### OBESITY PREVENTION IN AMERICAN INDIANS/ALASKA NATIVES: FIELD CENTER

NIH GUIDE, Volume 21, Number 31, August 28, 1992

RFA AVAILABLE: NIH-92-HL-08-P

P.T. 34, FE; K.W. 0715145, 0745027

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: October 15, 1992  
Application Receipt Date: December 18, 1992

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#### PURPOSE

The Division of Epidemiology and Clinical Applications (DECA) invites cooperative agreement applications for an estimated five Field Centers to participate [with the Coordinating Center, to be selected under a separate RFA: NIH-92-HL-09-P, and with the assistance of the National Heart, Lung, and Blood Institute (NHLBI)] in a collaborative study to assess the effectiveness of school-based intervention to prevent obesity in young American Indians/Alaska Natives (Native Americans). The solicitation is for the initial three-year planning and feasibility study of a planned nine-year effort.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Obesity Prevention in American Indians/Alaska Natives, is related to the priority areas of nutrition, physical activity fitness, educational and community-based programs, heart disease and stroke, and diabetes and chronic disabling diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Foreign organizations are not eligible to apply and domestic applications may not include international components. Applications from minority individuals, especially American Indians/Alaska Natives, and women are encouraged.

#### MECHANISM OF SUPPORT

The administrative and funding mechanism to be used to undertake this project will be a cooperative agreement, an assistance mechanism. Under the cooperative agreement, the NIH assists, supports, and/or stimulates and is involved substantially with recipients in conducting a study by facilitating performance of the effort in a "partner" role.

#### FUNDS AVAILABLE

An estimated five awards for Field Centers will be made under the RFA. A maximum of \$6.3 million (including direct and indirect costs) over a three-year period will be awarded for Field Centers and the Coordinating Center with at least two-thirds for Field Centers. First year total funding will be \$2.0 million.

#### RESEARCH OBJECTIVES

##### Background

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was rarely noted in Native Americans, but in the last decade, cardiovascular disease has become the leading cause of death in Native Americans. Several factors may be responsible for this increase, one of which is an increasing incidence of obesity. Reduction of the prevalence of obesity in Native Americans has been designated as a goal for improving the health of this minority population. The RFA attempts to address these issues with a project on primary prevention of obesity in young Native Americans.

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The objective of Phase II---not within the scope of the current awards, but relevant to the current RFA---will be to conduct a full-scale randomized intervention trial to prevent the development of obesity. It is envisioned that the intervention will be focussed on pre-adolescent elementary schoolchildren and that about 3000 Native American students study-wide will participate in intervention and control groups. Schools are expected to be the unit of randomization. An estimated six schools per center may be required in the full-scale study. The intervention is envisioned to last three to four years, depending on the time needed to show measurable difference in the selected obesity index between the intervention and control groups. (Note that this is not weight loss but a reduction in the rate of weight gain.) Data analysis and publication of study results will follow the completion of the intervention.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by October 15, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

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National Heart, Lung, and Blood Institute  
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Bethesda, MD 20892  
Telephone: (301) 496-7363  
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#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these awards. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441; and from the NIH Project Scientists named below.

Application must be received by December 18, 1992. An application not received by this date will be considered ineligible.

#### REVIEW CONSIDERATIONS

Applicants are encouraged to submit and describe their own ideas on how best to meet the goals of the study, but they are expected to address issues identified under SPECIAL REQUIREMENTS of the Request for Applications. NOTE THAT THIS DOCUMENT IS NOT THE REQUEST FOR APPLICATIONS. Applications will be judged primarily on the scientific quality of the application, the availability of a study sample with adequate numbers of students, evidence of a commitment of the Native American community to the proposed study and study investigators, the discussion of considerations relevant to the RFA, expertise of the investigators, their capability to perform the work proposed, and a demonstrated willingness to work together with other Centers and the NHLBI Project Scientists.

The review group will assess (as further detailed in the RFA):

- o Scientific merit of the study.
- o Plans to recruit schools and secure student, family and community participation.
- o Qualifications, experience, and commitment of key personnel.
- o Facilities, equipment and organizational structure to effectively implement intervention and data collection procedures.
- o Appropriateness of the budget for the work proposed.

#### AWARD CRITERIA

Applications recommended by the National Heart, Lung, and Blood Advisory Council will be considered for award based upon (a) scientific and technical merit and the requirements explicitly stated in the RFA, (b) program balance, including in this instance, sufficient compatibility of features to make a successful collaborative program a reasonable likelihood, and (c) availability of funds.

#### Time Table

Letter of Intent:	October 15, 1992
Application Receipt Date:	December 18, 1992
Review by National Heart, Lung, and Blood Advisory Council:	May, 1993
Anticipated Award Date:	July 1, 1993

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Requests for a copy of the RFA and inquiries regarding the announcement may be directed to:

Richard R. Fabsitz  
Clinical and Genetic Epidemiology Branch  
Division of Epidemiology and Clinical Applications  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3A17  
7750 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-4333

Direct fiscal and administrative matters to:

Marie Willett  
Deputy Chief, Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A12  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7255

#### AUTHORITY AND REGULATIONS

This project is described in the Catalog of Federal Domestic Assistance No. 93.837. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR 74. This project is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

NIH GUIDE, Volume 21, Number 31, August 28, 1992

RFA AVAILABLE: DA-93-01

P.T. 34; K.W. 0404009, 0710085, 0710100

National Institute on Drug Abuse

Application Receipt Date: December 11, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE GRANTS MANAGEMENT BRANCH IDENTIFIED IN INQUIRIES, BELOW.

#### PURPOSE

The Medications Development Division of the National Institute on Drug Abuse (NIDA) invites the submission of research applications to develop innovative preclinical (nonhuman) methods for the identification of potential treatment agents for the entire spectrum of cocaine abuse, from pre-addiction through abstinence, relapse, and recovery. The methods may be based on behavioral, neurophysiological, neurochemical, or other approaches as long as a strong case is made for relevance to human cocaine abuse and its pharmacologic treatment. These methods should be novel or expand other underdeveloped or unrecognized methods as tools for evaluating pharmacotherapies for drug abuse disorders.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, "The Development of Innovative Methods to Identify Medications for Treating Cocaine Abuse," is related to priority area of health promotion, alcohol and other drugs. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20492-9325 (telephone 202-783-3238).

#### ELIGIBILITY

Applications may be submitted by foreign and domestic, nonprofit and for-profit, public and private organizations such as universities, colleges, hospitals, laboratories, research institutions, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. Foreign applicants are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29).

#### MECHANISMS OF SUPPORT

Support mechanisms include the research projects (R01) and the FIRST Award (R29). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. For information on the special requirements of the FIRST Award (R29), contact the program staff listed at the end of the announcement. The total project period for applications submitted in response to the present RFA may not exceed five years for the R01 and R29.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures. R29 Awards may not be renewed, but awardees may apply for an R01.

#### FUNDS AVAILABLE

Applications submitted in response to this announcement will compete for approximately \$1,000,000 total costs that has been made available for this purpose in Fiscal Year 1993. It is expected that approximately four to five grants will be supported. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIDA, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The areas of research interest that may be funded include those that are innovative, that develop new methods of drug discovery for cocaine abuse pharmacotherapies, and that will advance the development of a new medication for the treatment of cocaine abuse. In general, these may include:

- o an innovative behavioral model of craving that does not employ the standard self-administration paradigms
- o models of behavioral toxicity that look at attenuation of important adverse effects of cocaine through a new approach
- o techniques to study post-addictive behavior as experimental models of recovery and possible relapse
- o neurophysiological techniques that utilize the putative underlying mechanisms of cocaine abuse to identify new medications
- o electrophysiological methods that will identify and develop new pharmacotherapeutic agents

These areas of research interest are not intended to be all-inclusive. However, experimental animal models to develop therapeutic interventions for cocaine abuse are extremely limited. Therefore, a major research effort is required to design innovative approaches to expand the current methods and models to those that have not been explored. Well-known models of drug abuse to study cocaine are of interest only insofar as the application constitutes an innovative approach. It is anticipated that no single method will be definitive and that both behavioral and non-behavioral techniques will be identified and developed.

#### STUDY POPULATIONS

This RFA is targeted for preclinical studies in non-human species, including rodents, monkeys, cell preparations from non-human sources. The PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions requires that applicant organizations establish and maintain appropriate policies and procedures to ensure the humane care and use of live vertebrates involved in research, research training, and biological testing activities supported by PHS. All institutions are required to comply, as applicable, with the Animal Welfare Act as amended (7 USC 2131 et seq.). These documents are available from the Office for Protection from Research Risks (OPRR), National Institutes of Health, Building 31, Room 5B59, Bethesda, MD 20892.

An applicant organization proposing to use vertebrate animals in PHS-funded studies must file an Animal Welfare Assurance Form with OPRR. As part of the Assurance, which commits the applicant organization to comply with PHS policy, the applicant organization must appoint an Institutional Animal Care and Use Committee (IACUC), which is required to review and approve those sections of application for PHS support that involve vertebrate animals. IACUC approval should be submitted at the time of application for studies which involve animal subjects.

If animal subjects will be involved at sites other than the applicant organization, the applicant must identify, within the application, the assurance status of each participant and must arrange the appropriate certifications and verifications.

#### APPLICATION PROCEDURES

Applicants must request the RFA, which contains additional information for applying under this RFA. Applications are to be submitted using the grant application form PHS 398 (rev. 9/91). Application kits containing the necessary forms and instructions for research grants may be obtained from business offices or offices of sponsored research at most universities, colleges, medical schools, and other major research facilities. If such a source is not available, the materials may be requested from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441.

Applications must be received by December 11, 1992. Applications received after each this date will be returned to the applicants without review.

#### REVIEW CONSIDERATIONS

Criteria for scientific/technical merit review of the applications will include the following:

- o Relevance of objectives to the goal of this program, as stated in the RFA including:
  - (a) Is the method innovative?
  - (b) Is the method workable as either a screening technique or as an evaluation technique?
  - (c) Will the method identify potential treatment agents?
- o Adequacy of the research design and methodology
- o Applicability of the project to clinical situations covering specific aspects of the addictive process from pre-addiction through craving, abstinence, relapse, and recovery
- o Potential contribution to the development of medications to treat cocaine abuse
- o Demonstrated scientific expertise of the Principal Investigator and other key personnel
- o Availability of adequate facilities, other resources, and collaborative arrangements necessary for the research
- o Appropriateness of budget estimates for the proposed research activities

#### AWARD CRITERIA

In making funding decisions, the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) and the NIDA will give consideration to availability of funds, potential contribution to the medications development program, overall scientific and technical merit as determined by peer review, needs and balances of the medications development portfolio, relevance to program goals and objectives, as stated in this RFA under RESEARCH OBJECTIVES.

#### INQUIRIES

Requests for the RFA and inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is encouraged.

Direct inquiries regarding programmatic issues to:

Heinz Sorer, Ph.D.  
Medications Development Division  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 11A-55  
Rockville, MD 20857  
Telephone: (301) 443-6270

Direct inquiries regarding fiscal matters to:

Shirley A. Denney  
Chief, Grants Management Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-55  
Rockville, MD 20857  
Telephone: (301) 443-6710

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, Number 93.279. Awards are made under authorization of the Public Health Service Act, section 301 and 515 (42 USC 241 and 290cc) and administered under PHS grants policies and Federal Regulations 42 CFR 92 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### CAREER DEVELOPMENT AWARDS FOR UNDERREPRESENTED MINORITY CLINICIAN-INVESTIGATORS

NIH GUIDE, Volume 21, Number 31, August 28, 1992

RFA AVAILABLE: DK-93-03

P.T. 34, FF; K.W. 0785035, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: November 4, 1992

Application Receipt Date: December 3, 1992

#### PURPOSE

The purpose of this solicitation is to increase the number of underrepresented minority clinicians who can conduct high-quality independent research and provide leadership in the areas of diabetes, endocrinology, metabolism and metabolic diseases, including cystic fibrosis; nutrition, eating disorders, obesity, organ systems and components associated with the gastrointestinal tract; renal and urological diseases, and hematology.

This Request for Applications (RFA) is limited to the Clinical Investigator Award (CIA/K08) and the Physician Scientist Award (PSA/K11). Each of these mechanisms is tailored to a particular stage of the investigator's career.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Career Development Awards for Underrepresented Minority Clinician-Investigators, is related to the priority area of nutrition and diabetes and chronic disabling disorders. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government.

Applicants for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) CIA and the NIDDK PSA must:

- o Hold an M.D., D.O., or other appropriate clinical degree;
- o Not have been a Principal Investigator on a PHS-supported research project; and
- o Commit at least 75 percent time to CIA activities.

In addition, applicants for the PSA must have completed at least one postgraduate year of clinical training by the time the award is made. Applicants for the CIA must have had approximately four to eight years of postdoctoral experience, both clinical and research (a minimum of two years of each) by the projected start of the award.



Potential candidates must be citizens or non-citizen nationals of the United States or its possessions and territories or must have been lawfully admitted to the United States for permanent residence at the time of the application and must be a member of a minority group that is underrepresented in biomedical or behavioral science.

Applicants applying for the CIA or the PSA under this solicitation must have completed, by the time an award would be activated, a residency in internal medicine, surgery, or pediatrics.

#### MECHANISMS OF SUPPORT

The mechanisms of support to be used are the Clinical Investigator Award (K08) and the Physician Scientist Award (K11). Detailed guidelines can be obtained from the office of sponsored programs at most research institutions or from the Office of Grants Inquiries, Division of Research Grants, NIH, telephone (301) 496-7441. Awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement.

#### FUNDS AVAILABLE

For FY 1993, the NIDDK plans to make up to a total of eight awards for applications submitted in response to this RFA. However, this funding level is dependent upon the receipt of a sufficient number of highly meritorious applications. Although this program is provided for in the financial plans of the NIDDK, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The objective of this solicitation is to increase the number of underrepresented clinicians who can conduct high-quality research and provide leadership in the areas of diabetes, endocrinology, metabolism and metabolic diseases, including cystic fibrosis; nutrition, eating disorders, obesity, organ systems and components associated with the gastrointestinal tract; renal and urological diseases, and hematology.

#### NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL STUDY POPULATIONS

It is NIH and ADAMHA policy that clinical research studies include women and minorities in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study. This policy is intended to apply to females and males of all ages. If women or minorities are excluded or inadequately represented in a clinical research project, particularly in proposed population based studies, a clear compelling rationale must be provided.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by November 4, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the applicant, the name of the sponsor, the names of all participating institutions, and the number and title of this RFA. However, a letter of intent is not required.

The letter of intent is to be sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91), is to be used in applying for the K awards. Special instructions for preparing CIA and PSA applications can be found in the booklet "The K Awards," October 1991. These forms and "The K Awards" booklet are available from most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants (address below) or call (301) 496-7441.

Applicants must submit a signed, typewritten original of the application, including the Checklist, and three signed exact photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At time of submission, two additional copies of the application must be sent under separate cover to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892

Applications must be received by December 3, 1992.

#### REVIEW CONSIDERATIONS

Applications will be reviewed initially by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NIDDK.

The review criteria for applications received in response to this RFA are the same as those for unsolicited K08 and K11 applications.

#### INQUIRIES

Written and telephone inquiries about this RFA and the opportunity to clarify any issues or questions from potential applicants are encouraged.

Direct requests and inquiries regarding programmatic issues to:

Lois F. Lipsett, Ph.D.  
Division of Diabetes, Endocrinology, and Metabolic Diseases  
Telephone: (301) 496-7433



#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.847, 93.848, and 93.849. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 66 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 32  
September 4, 1992

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES

NATIONAL HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 32, September 4, 1992

P.T. 42; K.W. 0783005, 1014006

National Institutes of Health  
Food and Drug Administration

The Office for Protection from Research Risks (OPRR) of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

SOUTHWESTERN WORKSHOP

DATES: November 16 & 17, 1992

LOCATION:

Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

SPONSORS:

University of Texas Health Science Center at Houston  
Prairie View A & M University



REGISTRATION:

Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

TITLE: Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

DESCRIPTION: Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, other health care professionals, clergy, lawyers, medical, nursing, social work students, and psychologists as well as IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

SOUTHEASTERN WORKSHOP

DATES: January 14 & 15, 1993

LOCATION:

Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

SPONSORS:

University of South Florida  
Florida A & M University

REGISTRATION:

Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

SOUTHWESTERN WORKSHOP

DATES: February 12 & 13, 1993

LOCATION:

Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

SPONSORS:

Arizona State University  
Northern Arizona University

REGISTRATION:

Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

TITLE: Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

DESCRIPTION: This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

For further information regarding these workshop or future NIH/FDA National Human Subject Protections Workshops, please contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

NOTICES OF AVAILABILITY (RFPs AND RFAs)

NIEHS CLINICAL TRIAL PROGRAM

NIH GUIDE, Volume 21, Number 32, September 4, 1992

RFP AVAILABLE: NIH-ES-92-34

P.T. 34; K.W. 0725005, 0755015

National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences (NIEHS) seeks to establish several contracts within 30 minutes' commuting distance of the NIEHS. The purpose is to provide clinical support services including access to patient facilities by NIEHS investigators performing clinical studies on the effect of environmental agents on human health. Examples of efforts to be explored under the contracts include the study of pulmonary pathobiological effects of environmentally induced asthma, studies of the role of in utero exposure of environmental estrogens on bone mineral density, and studies of the role of environmental estrogens on the onset and progression of puberty in children. Specific studies will be identified by Task Orders. The requirement

for geographic proximity will allow NIEHS investigators to coordinate their research efforts by physically working at several sites (NIEHS and contractor facilities) on a frequent basis. It is anticipated that several awards will be made. The estimated period of performance is 10 years. Release of the Request for Proposals (RFP) is anticipated on or about September 2, 1992, with proposals due October 20, 1992. All responsible sources may submit a proposal that shall be considered by the agency.

Requests must reference RFP NIH-ES-92-34 and must be forwarded to:

National Institute of Environmental Health Sciences  
Contracts and Procurement Management Branch, OM  
ATTN: Thomas M. Hardee, Contracting Officer  
79 TW Alexander Drive, Building 4401 Research Commons  
P.O. Box 12874  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7893  
FAX: (919) 541-2712

#### POSSIBLE ROLE OF METALLOTHIONEIN IN CARCINOGENESIS

NIH GUIDE, Volume 21, Number 32, September 4, 1992

RFA AVAILABLE: CA-92-22

P.T. 34; K.W. 0715035, 1007009, 1003018, 1002008, 0710030

National Cancer Institute

Letter of Intent Receipt Date: October 2, 1992

Application Receipt Date: December 8, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE COMPLETE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

#### PURPOSE

The Chemical and Physical Carcinogenesis Branch, Division of Cancer Etiology, National Cancer Institute (NCI), in collaboration with the Cancer Biology Branch, Division of Cancer Biology, Diagnosis, and Centers, NCI, and the Grants and Contracts Operations Branch, Division of Cancer Treatment, NCI, invites investigator-initiated research grant applications to elucidate the possible role of metallothionein (MT) in carcinogenesis. In addition, the National Institute of Environmental Sciences (NIEHS) has an interest in the general topic of metallothionein, but not in the specific emphasis of this RFA, which is the possible role of metallothionein in carcinogenesis. New and experienced investigators may apply for research funds to pursue multidisciplinary research projects.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Possible Role of Metallothionein in Carcinogenesis, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone 202-783-3238.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from women and minority investigators are encouraged.

#### MECHANISM OF SUPPORT

Support of this program will be through the National Institutes of Health (NIH) traditional research project grant (R01). Applicants will be responsible for the planning, direction, and execution of the proposed project. The total project period may not exceed four years.

## FUNDS AVAILABLE

Total costs of \$1,500,000 per year for four years will be committed to specifically fund applications submitted in response to this RFA. It is anticipated that 9 to 11 awards will be made contingent upon the availability of funds. The earliest feasible start date for the initial awards will be July 1, 1993.

## RESEARCH OBJECTIVES

The objectives of this RFA are to encourage research designed to elucidate the possible role of MT in carcinogenesis. Specific topic areas that might be supported by the RFA include, but are not limited to:

- o Biological and toxicological roles of MT. Studies such as metal homeostasis, detoxification, transport, role in cell proliferation during the perinatal period, and involvement of zinc as a second messenger in signal transduction, as related to cellular normality.
- o Regulation of MT gene expression. Studies of metal induction in various tissues, during development, and organismal specificity in transgenic and model systems and in normal versus transformed cells.
- o Role of MT in tumor cell pathobiology. Studies to define the role of MT in tumor cell progression and metastasis and the types and staging of tumors that may or may not express excess MT. Studies directed at enhancing a rational basis for therapeutic intervention with metallic anticancer drugs.
- o Role of MT in cancer chemotherapy. Studies on the role of MT in tumor cell resistance to anticancer drugs, especially metal-based drugs. Studies on the use of induction of MT in non-tumor tissue as an adjunct to reduce toxicity for metallic chemotherapeutics. Studies involving mechanisms by which MT synthesis could be specifically depressed in tumor cells to make them hypersusceptible to metallic chemotherapeutics.
- o Susceptibility factors in metal carcinogenesis. Studies assessing MT gene expression in target tissues of metallic carcinogens in rodents and molecular epidemiology of MT with special emphasis on target tissues of metallic carcinogens in humans (e.g. prostate, lung).
- o Molecular interaction of MT with ligands (metals and anticancer drugs) including binding and exchange, and structural and dynamic studies.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Each prospective applicant is asked to submit, by October 2, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, telephone and FAX numbers of the PI, the names of other key personnel, the participating institution(s), and the number and title of the RFA in response to which an application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, it contains information that is helpful in planning for the review. The letter of intent allows NCI staff to estimate the potential review workload and helps to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Yung-Pin Liu  
Program Director, Carcinogenesis Mechanisms  
Chemical and Physical Carcinogenesis Branch  
Division of Cancer Etiology  
National Cancer Institute  
Executive Plaza North, Suite 700  
Bethesda, MD 20892  
Telephone: (301) 496-5471  
FAX: (301) 496-1040



#### APPLICATION PROCEDURES

Applications must be received by December 8, 1992. The research grant application form PHS 398 (rev. 9/91) is to be used in applying for awards under this RFA. The application package is available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892; telephone 301/496-7441; and from the NCI Program Director named above.

#### REVIEW CONSIDERATIONS

Those applications will be evaluated according to the review criteria stated in the RFA for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board will consider the special needs of the NCI and the priorities of the National Cancer Program.

#### INQUIRIES

This Notice of Availability is an abbreviated version of the RFA. Copies of the complete RFA and written and telephone inquiries concerning the objectives and scope of the RFA are to be directed to Dr. Liu at the above address.

Written and telephone inquiries of a budgetary, administrative, and/or policy nature are to be directed to:

Ms. Jean Cahill  
Grants Management Team Leader  
Grants Administration Branch  
National Cancer Institute  
Executive Plaza South, Suite 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800, ext. 47  
FAX: (301) 496-8601

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.393, Cancer Cause and Prevention Research. Awards are made under the authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### BIOMARKERS OF DIETARY FAT IN POST-MENOPAUSAL WOMEN

NIH GUIDE, Volume 21, Number 32, September 4, 1992

RFA AVAILABLE: CA-92-14

P.T. 34; K.W. 0710095, 0760003, 0765025

National Cancer Institute

Letter of Intent Receipt Date: October 7, 1992

Application Receipt Date: January 26, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Cancer Prevention and Control, National Cancer Institute (NCI), invites applications for cooperative agreements directed towards the identification and evaluation of potential biochemical/biological markers to assess total dietary fat intake in post-menopausal women and to monitor adherence to dietary interventions in cancer prevention clinical trials.

The purpose of this RFA is to encourage the submission of applications from qualified investigators interested in conducting investigations designed to identify, characterize, and evaluate biochemical/biological markers to assess dietary intake and adherence. This research initiative also seeks to identify and establish a network

of institutions and organizations with scientific expertise, facilities, and capabilities to conduct controlled feeding studies, metabolic studies, and field studies.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Biomarkers of Dietary Fat in Post-Menopausal Women, is related to the priority area of cancer prevention. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or "Healthy People 2000" Summary Report: Stock No. 017-001-0043-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will support awards through the cooperative agreement, an assistance mechanism in which substantial NCI programmatic involvement with the recipient during performance of the planned activity is anticipated. The nature of NCI staff involvement is described in the RFA. Applicants will be responsible for the planning, direction, and execution for the proposed project. In addition to the requirements stated in this RFA, awards will be administered under PHS grants policy as stated in Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, (rev. 10/90).

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed by the Division of Research Grants (DRG). If the NCI determines that there is a sufficient continuing program need, the NCI may invite all funded recipients to submit competing continuation applications.

#### FUNDS AVAILABLE

Approximately \$750,000 in total costs per year for three years will be committed to fund applications submitted in response to this RFA. It is anticipated that three to five awards will be made. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications submitted in response to the present RFA may not exceed three years. Although this program is provided for in the financial plans of the NCI, the award of grants pursuant to this RFA is also contingent upon the continuing availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The specific objectives of this RFA are to encourage research on the identification and evaluation of biochemical/biological indicators of total dietary fat intake in post-menopausal women on self-selected low- and high-fat diets and in controlled feeding and/or metabolic studies.

#### Background

A major challenge in studying the effects of diet on health and chronic disease risks is the difficulty of assessing dietary intake. Current methods for dietary assessment and adherence monitoring have different levels of precision and accuracy and all have the inherent limitation of relying on self-reported data. The availability of biochemical/biological markers for assessing dietary fat intake and adherence in post-menopausal women would greatly facilitate the design, conduct, and interpretation of cancer prevention clinical trials, analytical epidemiologic studies, and diet-health survey studies on the relationship of diet and cancer risk. Identification of biochemical/biological indicators of dietary exposure would circumvent the current dietary assessment methodological shortcomings that limit the interpretation of data and often prevent the derivation of precise conclusions about the association of dietary patterns and/or specific dietary components with the risk of cancer and other chronic diseases.

Specific and sensitive biochemical/biological indicators of dietary intake, in particular total dietary fat, would greatly facilitate the design, conduct and interpretation of dietary intervention trials, epidemiologic studies and diet-health survey studies that attempt to determine the role of diet in cancer risk and prevention. In studies involving dietary modifications, the extent to which the results may be influenced by varying degrees of adherence is an aspect that is both important and difficult to evaluate. Thus, evaluation and validation of potential biochemical/biological indices of dietary intake will require controlled human feeding studies using well-defined diets and precise measures of actual intake.

## Studies of Special Interest

Specifically, applications are solicited that will (1) identify and evaluate potential biochemical/biological indicators of adherence in post-menopausal women on self-selected low- and high-fat diets, and/or (2) identify and evaluate biochemical/biological indicators of adherence to low-fat diets in post-menopausal women in controlled feeding and/or metabolic studies. Applicants may propose also to conduct a series of short-term (6-12 weeks) controlled clinical and/or metabolic studies and/or field studies. These studies should be designed to identify, characterize, and evaluate minimally invasive, specific and sensitive biochemical/biological indicators for assessing total fat intake and/or for monitoring adherence to low-fat diets. Emphasis should be focused on dietary patterns that are nutritionally adequate and are characterized by reduced levels of total fat and saturated fat, increased levels of complex carbohydrates and fiber, and include a variety of foods typically present in the U.S. diet. In addition, the influence of varying the levels of fat intake while keeping fiber intake constant, weight loss, and energy balance may be taken into consideration in the study designs.

## SPECIAL REQUIREMENTS

The RFA describes the complete terms for this cooperative agreement, including terms of cooperation, responsibilities of the NCI Program Director, responsibilities of the awardees, and the arbitration process to resolve disputes. Other required applicant information and special instructions for preparation of cooperative agreement applications are also included.

## STUDY POPULATIONS

### SPECIAL INSTRUCTION TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of minorities in study populations. If minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit by October 7, 1992, a letter of intent that includes a descriptive title of the proposed research, the name and address of the PI, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, it is requested in order to provide an indication of the number and scope of applications to be reviewed.

The letter of intent is to be sent to:

### Postal Mail Address:

Carolyn K. Clifford, Ph.D.  
Diet and Cancer Branch  
Division of Cancer Prevention and Control  
National Cancer Institute  
Executive Plaza North, Room 212  
Bethesda, MD 20892-6130  
Telephone: (301) 496-8573  
FAX: (301) 402-0553

### Overnight Delivery Address:

Carolyn K. Clifford, Ph.D.  
Diet and Cancer Branch  
Division of Cancer Prevention and Control  
National Cancer Institute  
6130 Executive Boulevard  
Executive Plaza North, Room 212  
Rockville, MD 20852

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892; telephone 301/496-7441 and from the NCI Program Director named below.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the program requirements and criteria stated in the RFA is an NCI program staff function. Applications that are judged non-responsive will be returned to the applicant, but may be submitted as investigator-initiated research grants. Questions concerning the responsiveness of proposed research to the RFA should be directed to program staff (see INQUIRIES).

If the number of applications is large compared to the number of awards to be made, the NCI may conduct a preliminary scientific peer review (triage) to eliminate those applications that are clearly not competitive. The NCI will remove from competition those applications judged to be noncompetitive for award and notify the applicant and institutional business official. Those applications judged to be both competitive and responsive will be further evaluated according to the review criteria stated in the RFA for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board considers the special needs of the NCI and the priorities of National Cancer Program.

## AWARD CRITERIA

The anticipated date of award is September 30, 1993. Awards made pursuant to this RFA are contingent upon the availability of funds for this purpose and the scientific review.

## INQUIRIES

The program staff welcome the opportunity to clarify any issues or questions from potential applicants. Written and telephone inquiries concerning the objectives and scope of this RFA, inquiries about specific proposed research, and requests for the RFA are encouraged and should be directed to the Program Director listed below.

Direct inquiries regarding programmatic issues to:

Carolyn K. Clifford, Ph.D.  
Chief and Program Director  
Diet and Cancer Branch  
Division of Cancer Prevention and Control  
National Cancer Institute  
Executive Plaza North, Room 212  
Bethesda, MD 20892-6130  
Telephone: (301) 496-8573  
FAX: (301) 402-0553

Direct inquiries regarding fiscal matters to:

Eileen Natoli  
Team Leader, PC Team  
Grants Administration Branch  
National Cancer Institute  
6120 Executive Boulevard  
Executive Plaza South, Room 243  
Rockville, MD 20852  
Telephone: (301) 496-7800, ext. 56

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.399, Cancer Control. Awards will be made under the authority of the Public Health Services Act, Title IV, Section 301 (Public Law 78-410, 42 U.S.C. 241 and Section 412, as amended by Public Law 99-518, 42 U.S.C 258a-1); and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12732 or Health Systems Agency review.



## ONGOING PROGRAM ANNOUNCEMENTS

### RESEARCH ON MENTAL HEALTH SERVICES IN GENERAL HEALTH CARE

NIH GUIDE, Volume 21, Number 32, September 4, 1992

PA NUMBER: PA-92-103

P.T. 34; K.W. 0715129, 0730050

National Institute of Mental Health

#### PURPOSE

The goal of this Program Announcement (PA) is to encourage research on mental disorders in primary care and other general medical settings, particularly research that focuses on the nature, recognition, classification, treatment, and outcomes of people with mental disorders in these service settings. This announcement may encourage the development of needed research that seeks to improve understanding of how best to assess mental disorders and provide mental health services in general health care settings.

Among people with current mental disorders who use health services, about half are not treated in the specialty mental health care sector and receive health services only in general medical settings. While investigator-initiated research in this area has grown substantially, there is still a tremendous dearth of accurate information on the kinds of patients with mental disorders in the general health care sector, the nature and severity of their disorders, and the relationship of these mental disorders to medical conditions, as well as on the mental health services--- types, quality, effectiveness---delivered in primary care and other general health care sectors (e.g., emergency rooms, nursing homes, general hospital medical and surgical units, rehabilitation hospitals).

The Primary Care Research Program at the National Institute of Mental Health (NIMH) was established in response to research findings indicating the relative gap in use of specialty mental health services compared to primary care service use by people with mental disorders, and as an attempt to understand the low recognition rates of mental disorders in general medical settings and to contribute to health care policy. While major research issues at the outset included epidemiological (prevalence and types of disorders), nosologic (validity and reliability of diagnoses), clinical practice and services, systems/organizational, and economic questions, existing research data are still scant in most of these areas, despite a growth in the field's scientific inquiries and related activities sponsored by the program. Furthermore, this research is called for by the mental health objectives in the recent report "Healthy People 2000"---two of which directly address the provision of mental health services by primary care providers (6.13, 6.14) [footnote 1]. Other recent activities---the Agency for Health Care Policy and Research of guidelines for the treatment of depression in primary care (with which the NIMH has been involved) [footnote 2] active work with new classification of mental disorders in primary care [footnote 3]---support this effort.

These and other activities [footnote 4], aligned with scientific data on the impact of mental health on overall functioning and disability in people seen in the general health care sector [footnote 5] make a strong call for more scientific inquiry to inform the gaps between the mental health needs seen in these general sector settings and the services provided in these settings.

These gaps are even more evident in special populations seen mainly in the general health care sector and the special issues of access, assessment, and utilization that are unique to them: rural groups, minority populations, inner city groups, and HIV-infected people. Attention should also be given to unique issues related to women, children, adolescents, and the elderly.

Last, research is strongly needed on those people with mental disorders who may need more services in the general health sector, particularly the severely mentally ill [footnote 6] and the homeless.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This effort is in accordance with specific objectives 6.13 and 6.14. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone (202) 783-3238.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, public and private, non-profit and for-profit organizations, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply. Foreign institutions are only eligible for traditional research grants.

## MECHANISMS OF SUPPORT

Research support may be requested through applications for traditional research grant (R01), a small grant (R03), and First Independent Research Support and Transition (FIRST) Award (R29). Since the latter programs have special requirements, applicants are advised to refer to specialized announcements for the small grant and FIRST award programs, available from:

National Institute of Mental Health  
Division of Extramural Activities  
Office of Extramural Policy and Analysis  
5600 Fishers Lane, Room 9-97  
Rockville, MD 20857  
Telephone: (301) 443-4673

### Terms and Conditions of Support

Grant funds may be used for expenses clearly related and necessary to conduct the proposed research, including direct costs and allowable indirect costs.

### Period of Support

Applications for traditional research projects may request support for up to five years. Small grants are limited to two years and may not be renewed. FIRST awards are made for five years, but are not renewable. Annual awards will be made, subject to continued availability of funds and progress achieved. A competing continuation (renewal) application for a traditional research award (R01) may be submitted before the end of an approved period of support in order to request funds for the continuation of the project.

## RESEARCH OBJECTIVES

The following list of research objectives is meant to be exemplary and not exhaustive---it serves to identify key topics in which further rigorous scientific research is needed to delineate mental health needs and to assess the mental health services provided in the general health care sector:

### (1) Methodological Issues

- o Studies of classification systems for mental disorders and treatments delivered in the general health care sector, with special emphasis on validity, comparative diagnostic assessments, and clinical problems not addressed by available nosologic systems (e.g., childhood behavioral disorders, subsyndromal disorders like minor depression or mixed anxiety-depression)
- o Research on the development, applicability, and utility of instruments or analytic techniques that may be used to assess multi-dimensional outcomes for people with both mental and medical disorders seen in the general health care sector. Such outcomes might include severity of illness, disability, costs, and community and family burden
- o Research on the applicability and utility of existing mental health screening, diagnostic and management instruments in primary care settings, particularly among patients from different socio-economic, ethnic, and cultural backgrounds
- o Studies using innovative methodologies (e.g., decision analysis, meta-analysis) to examine the clinical management of people with mental disorders in the general health care sector

### (2) Recognition and Diagnosis

- o Studies examining the presentation and nature of mental disorders in primary care and other general health care settings (especially for children and the elderly), especially duration, remission, and recurrence of these disorders, with special consideration to the longitudinal evaluation of treated and untreated subsyndromal conditions that impair health status

- o Studies of the impact of co-occurring general medical illnesses on the accurate assessment of mental disorders, and impact on mental health services delivered in the general health sector for these populations (e.g., the "accurate" assessment of depression in the medically ill and service implications)

- o Studies of the relationship between co-occurring alcohol or drug problems and mental disorders, and the impact of these conditions on accurate recognition of mental problems by general health care providers

- o Studies of the barriers to the accurate recognition and diagnosis of mental disorders, especially in primary care, with special attention to (a) patient variables such as population specific beliefs (e.g., rural, cultural) and (b) provider variables, such as knowledge and attitudes about mental disorders, which may impact on recognition and management of people with mental disorders

### (3) Clinical Services and Practices

- o Research on the types, quality and effectiveness of mental health services provided by general health care providers, differences of these services in relation to type of patient (e.g., understudied groups like the elderly and women in various life cycle stages who seek general health care), provider (e.g., physician, nurse, social worker) and setting, and impact on patient outcomes

- o Studies of referral patterns from the general health care sector to the mental health care sector and barriers to referral (e.g., access, attitudes, training, reimbursement)---rates, processes, and effect on patient outcomes, as well as strategies to overcome those barriers

- o Studies addressing improvement of current clinical practice to ensure adequate mental health services in the general health care sector---application of clinical trials, analysis of provider-patient interactions, feasibility of transferring specialist mental health services to general health care settings, and consultation-liaison models

- o Studies of innovative educational/teaching models to improve the recognition and care of patients with mental disorders by their general health care service providers (e.g., utility of clinical practice guidelines)

### (4) Service System and Financing Issues

- o Studies of the organization, delivery, and cost-effectiveness of services for mental conditions in primary care settings, with focus on variations in practice (e.g., managed care systems) and setting (e.g., rural, community health centers)

- o Research on the impact of different reimbursement approaches on the use of general health vs. mental health services (e.g., prepaid health plans) and implications for services, quality of care, and patient outcomes

- o Research on existing or innovative models linking or integrating mental health services with the general health care sector, particularly for people with severe mental disorders and/or who are homeless, whose needs crosscut different systems of care (e.g., state consolidated funding for continuous, coordinated health and social services)

- o Studies examining the nature and effectiveness of relationships between the general health care sector and other systems (e.g., educational, legal, community) in providing mental health services

## STUDY POPULATIONS

### Protection of Human Subjects

The Department of Health and Human Services has regulations for the protection of human subjects and has developed additional regulations for the protection of children. A copy of these regulations (45 CFR 46, Protection of Human Subjects) and those pertaining specifically to children are available from the Office for Protection from Research Risks, National Institutes of Health, Bethesda, MD 20892, telephone (301) 496-7041. Specific questions concerning protection of human subjects in research may be directed to NIMH staff members listed under INQUIRIES.

### NIH POLICY CONCERNING INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

Applications for grants and cooperative agreements that involve human subjects are required to include minorities and both genders in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages. If one gender and/or minorities are excluded or are inadequately represented in this research, particularly in proposed population-based studies, a clear compelling rationale for exclusion

or inadequate representation should be provided. The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., American Indians or Alaskan Natives, Asians or Pacific Islanders, Blacks, Hispanics). Investigators must provide the rationale for studies on single minority population groups.

Applications for support of research involving human subjects must employ a study design with minority and/or gender representation (by age distribution, risk factors, incidence/prevalence, etc.) appropriate to the scientific objectives of the research. It is not an automatic requirement for the study design to provide statistical power to answer the questions posed for men and women and racial/ethnic groups separately; however, whenever there are scientific reasons to anticipate differences between men and women, and racial/ethnic groups, with regard to the hypothesis under investigation, applicants should include an evaluation of these gender and minority group differences in the proposed study. If adequate inclusion of one gender and/or minorities is impossible or inappropriate with respect to the purpose of the research, because of the health of the subjects, or other reasons, or if in the only study population available, there is a disproportionate representation of one gender or minority/majority group, the rationale for the study population must be well explained and justified.

The NIH funding components will not make awards of grants and cooperative agreements that do not comply with this policy. For research awards which are covered by this policy, awardees will report annually on enrollment of women and men, and on the race and ethnicity of subjects.

#### APPLICATION PROCEDURES

Applicants are to use the Public Health Service research grant application form PHS 398 (rev. 9/91). The number and title of this announcement, PA-92-103, Research on Mental Health Services in the General Health Care Sector, must be typed in item number 2a on the face page of the PHS 398 application form.

Application kits containing the necessary forms may be obtained from business offices and offices of sponsored research at most universities, colleges, medical schools, and other major research facilities. If such a source is not available, the following office may be contacted for the necessary application material:

Grants Management Branch  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C-05  
Rockville, MD 20857  
Telephone: (301) 443-4414

The signed original and five legible copies of the completed application must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by the assigned review group in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate national advisory council.

Review criteria include:

- o Scientific, technical, or medical significance and originality of the proposed research;
- o Appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;
- o Qualifications and research experience of the Principal Investigator and staff, particularly but not exclusively in the area of the proposed research;
- o Availability of resources necessary to perform the research, and
- o Appropriateness of the proposed budget and duration in relation to the proposed research.



Applications will be reviewed in accordance with the following review schedule:

Receipt Dates New/Renewal	Initial Review	Advisory Council Review	Earliest Start Date
Feb 1/Mar 1*	May/Jun	Sep/Oct	Dec 1
Jun 1/Jul 1*	Oct/Nov	Jan/Feb	Apr 1
Oct 1/Nov 1*	Feb/Mar	May/Jun	Jul 1

\*Competing continuations, supplemental, and revised applications are to be submitted on these dates.

Applications received after a given receipt date will be held for the next scheduled receipt date or returned to the applicant, if so requested by the applicant, without review.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions: quality of the proposed project as determined by peer review, availability of funds, and program balance among research areas of the announcement.

#### INQUIRIES

NIMH staff are available for consultation concerning application development before or during the process of preparing an application. Potential applicants are advised to contact NIMH staff as early as possible for information and assistance in initiating the application process and developing an application.

Direct inquiries regarding programmatic issues to:

Junius J. Gonzales, M.D.  
Chief, Primary Care Research Program  
Services Research Branch  
Division of Applied and Services Research  
National Institute of Mental Health  
5600 Fishers Lane, Room 18C-14  
Rockville, MD 20857  
Telephone: (301) 443-1330

Direct inquiries regarding fiscal matters to:

Stephen J. Hudak  
Chief, Grants Management Section  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C-23  
Rockville, MD 20857  
Telephone: (301) 443-4456

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.242. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. Applications submitted in response to this announcement are not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### FOOTNOTES

1. Healthy People 2000, DHHS Publication No. (PHS) 91- 50212. Potential applicants may obtain a copy of Healthy People 2000 (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: (202) 783-3238).

2. AHCPR Panel on Guidelines for the Treatment of Depression in Primary Care.

3. NIMH Workshops on the Classification of Mental Disorders in Primary Care, 1989-90.

4. Primary Care Research: Theory and Practice, Conference Proceedings, Agency for Health Care Policy and Research Publication No. 91-011.



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5. Wells KB et al. The functioning and well-being of depressed patients: Results from the medical outcomes study. Jour. Amer. Med. Assoc. 262: 914-919, 1989.

6. Caring for People With Severe Mental Disorders: A National Plan of Research to Improve Services, DHHS Publication No. (ADM) 91-1762.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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## For Grants and Contracts

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**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

**Vol. 21., No. 33**  
**September 11, 1992**

RICHARD W. URB

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29 WILD FOREST DRIVE  
GAITHERSBURG MD 20878-0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

## NOTICES

### NATIONAL HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 33, September 11, 1992

P.T. 42; K.W. 0783005, 1014006

National Institutes of Health  
Food and Drug Administration

The Office for Protection from Research Risks (OPRR) of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

#### SOUTHWESTERN WORKSHOP

DATES: November 16 & 17, 1992



LOCATION:  
Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

SPONSORS:  
University of Texas Health Science Center at Houston  
Prairie View A & M University

REGISTRATION:  
Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

TITLE: Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

DESCRIPTION: Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, other health care professionals, clergy, lawyers, medical, nursing, social work students, and psychologists as well as IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

#### SOUTHEASTERN WORKSHOP

DATES: January 14 & 15, 1993

LOCATION:  
Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

SPONSORS:  
University of South Florida  
Florida A & M University

REGISTRATION:  
Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

#### SOUTHWESTERN WORKSHOP

DATES: February 12 & 13, 1993

LOCATION:

Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

SPONSORS:

Arizona State University  
Northern Arizona University

REGISTRATION:

Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

TITLE: Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

DESCRIPTION: This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

For further information regarding these workshop or future NIH/FDA National Human Subject Protections Workshops, please contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

RESEARCH CAREER DEVELOPMENT AWARD PROGRAM FOR RE-ENTRY INTO THE NEUROLOGICAL SCIENCES

NIH GUIDE, Volume 21, Number 33, September 11, 1992

P.T. 34; K.W. 1002030, 0785035

National Institute of Neurological Disorders and Stroke

The purpose of the National Institute of Neurological Disorders and Stroke (NINDS) program for re-entry into the neurological sciences is to assist basic and clinical neurological scientists to re-enter into active careers in science and academic medicine related to the neurological sciences. The program is designed to provide the re-entry opportunity to individuals who have experienced an interruption of three to eight years in their careers. It is a postdoctoral award (K01) designed to support individuals who would have high potential for careers as independent investigators in basic or clinical research in the neurological sciences following a period of support that will allow the individual to update his/her research skills. These awards would allow the individual to pursue a research project that would enable him/her to update research skills, learn new techniques, and obtain any other experience necessary. This effort may be complemented by taking courses appropriate to the research objectives of the award. The award provides salary for the awardee of up to \$50,000 per year and a research allowance of up to \$20,000 per year.

To obtain a copy of the program guidelines, please contact:

Mr. Edward M. Donohue  
Deputy Director  
Division of Extramural Activities  
National Institute of Neurological Disorders and Stroke  
Bethesda, MD 20892  
Telephone: (301) 496-4188

NIH GUIDE, Volume 21, Number 33, September 11, 1992

P.T. 36; K.W. 0780010

#### Public Health Service

This announcement is a revision of the one last appearing in the NIH Guide for Grants and Contracts on September 16, 1988, Vol. 17, No. 29, pages 1 and 2. This revised notice contains a number of changes in policy that the agencies of the Public Health Service (PHS) have determined should be implemented.

Investigators conducting biomedical research frequently develop unique research resources. Categories of these resources include: synthetic compounds, organisms, cell lines, viruses, cell products, cloned DNA, as well as DNA sequences, mapping information, crystallographic coordinates, and spectroscopic data. Some specific examples are: specialized and/or genetically defined cell lines, including normal and diseased human cells; monoclonal antibodies; hybridoma cell lines; microbial cells and products; viruses and viral products; recombinant nucleic acid molecules; DNA probes; nucleic acid and protein sequences; certain types of animals such as transgenic mice; and intellectual property such as computer programs. The PHS provides the following statement of policy concerning unique research resources developed through PHS awards.

#### A. Policy on Distribution of Research Resources

The policy of the PHS is to make available to the public the results and accomplishments of the activities that it funds. Restricted availability of unique resources upon which further studies are dependent can impede the advancement of research and the delivery of medical care. Therefore, when these resources are developed with PHS funds and the associated research findings have been published or after they have been provided to the agencies under contract, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. This policy applies to PHS intramural investigators as well as extramural scientists funded by PHS grants, cooperative agreements, and contracts.

Because of concern that some crystallographers are not making their coordinates available promptly (see Science, Vol. 245, p. 1179), one of the national advisory councils of the NIH and the executive committee of another institute recently adopted resolutions affirming the policy of the International Union of Crystallographers (IUCr) (Acta Cryst., A45: 658, 1989). The PHS has now adopted the IUCr policy that includes data from publications based on spectroscopic data such as nuclear magnetic resonance as well as crystallographic coordinates.

The PHS encourages investigators who have such resources to consult the appropriate Program Administrators who may be of assistance in determining a suitable distribution mechanism. Such a mechanism should take into consideration all applicable Federal regulations including, but not limited to: those regarding human subjects, animal welfare, and use and handling of hazardous materials, where applicable. Investigators requesting materials should provide evidence of having the proper training, experience, and facilities to make use of the items they request. Program staff of the agencies will be available to assist in verification of credentials of requesters where such concern exists on the part of suppliers.

Investigators who believe that they will be unable to implement this policy should promptly contact the appropriate PHS Program Administrator to discuss the circumstances, obtain information that might facilitate compliance with the policy, and reach an understanding in advance of the subsequent award. For research and development contracts, approval should be obtained from the PHS Contracting Officer before distribution of unique resources, unless the terms of the contract permit distribution without prior clearance of the Contracting Officer. In order to facilitate the availability of unique or novel biological materials and resources developed with PHS funds, investigators may distribute the materials through their own laboratory or institution or submit them, if appropriate, to entities such as the American Type Culture Collection or other repositories. In the case of unique biological information, such as DNA sequences or crystallographic coordinates, investigators are expected to submit them to the appropriate data banks because they otherwise are not truly accessible to the scientific community. When distributing unique resources, investigators are to include pertinent information on the nature, quality, or characterization of the materials.

Investigators must exercise great care to ensure that resources involving human cells or tissues do not identify original donors or subjects, directly or through identifiers, such as codes linked to the donors or subjects.

The goals of some programs, (e.g., the Human Genome Program) are such that applicants for certain projects may be required to provide plans for the sharing of data and materials. These plans will undergo review by program staff and the national advisory council prior to award.

#### B. Distribution Costs

Institutions and investigators may charge the requester, if necessary, for the reasonable cost of production of unique biological materials, and for packaging and shipping. Such costs may include labor, supplies, and other directly related expenses. Investigators should note, however, that such a charge accrues as general program income. This should not be an impediment to the distribution of materials, but investigators and institutions are advised that:

a) for grants, the income is governed by 45 CFR Part 74 and it must be reported on the Financial Status Report. Questions regarding these policies and the treatment of income should be directed to the Grants Management

Officer.

b) for contracts, the income is governed by Federal Acquisition Regulations (FAR) 45.610-3. Contracting Officers must be contacted before generating any revenues from the distribution of materials. Any contract under which research resources would be sold require specific contract instructions. Existing contracts may require an amendment and specific approval of the Contracting Officer to render them allowable.

#### C. Inventions and Commercialization

Federal policy encourages the commercialization of the products of research developed as a consequence of Federal funding; therefore, the intent of this policy is to not discourage, impede, or prohibit the organization that develops unique research resources or intellectual property from commercializing the products. Investigators may make their materials available to others for commercial purposes with appropriate restrictions and licensing terms as they and their institution deem necessary.

Institutions are reminded that some of these products may be inventions subject to the various laws and regulations applicable to patents and must be reported to the Extramural Inventions Reports Office of the NIH. The terms for licensing of unpatented research products, such as cell lines, monoclonal antibodies, and other materials and products, should generally be no more restrictive than would have been the case had they been patented--for example, only if there is full public disclosure of the invention/discovery, availability through a repository, and written agreement to end all fees and constraints after 17 years. When reporting is required, it should occur at the earliest possible time. (See 37 CFR 401 and NIH Guide for Grants and Contracts, Vol. 19, No. 6, February 9, 1990, page 2).

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

##### SYNTHESIS OF CHEMICAL MODIFIERS OF RADIATION RESPONSE

NIH GUIDE, Volume 21, Number 33, September 11, 1992

RFP AVAILABLE: NCI-CM-37828-75

P.T. 34; K.W. 0745062, 1003006, 0755025

National Cancer Institute

The Radiotherapy Development Branch, Radiation Research Program, Division of Cancer Treatment, National Cancer Institute is seeking organizations with the capability to design, synthesize, and characterize new and novel chemical modifiers of radiation response. Classes of interest are: bioreductive agents, agents that exploit tumor pathophysiology, inhibitors of repair of radiation damage, and free radical base agents. The project requires designated data obtained from in vitro testing of synthesized compounds and data regarding the efficacy in vivo of designated compounds with significant activity in vitro.

The offeror should include an experienced radiobiologist and an experienced synthetic organic chemist on the project team, and the Principal Investigator should possess a doctorate in a relevant science. In addition, the offeror must be AAALAC accredited or equivalent and be capable of maintaining a conventional rodent colony of at least 400 mice. The offeror must also have radiation capability suitable for irradiating mice and cell cultures. Equipment for physicochemical and pharmacological analysis (e.g., UV, IR, NMR, HPLC, and polarographic or pulse radiolysis for measuring electron affinity, when appropriate) of compounds to be synthesized is also required.

RFP No. NCI-CM-37828-75 will be issued, upon written request to Bernice Evans, Contract Specialist, on or about August 10, 1992, with a due date for receipt of proposals on December 15, 1992. It is anticipated that an incrementally funded contract will be awarded for a period of four years beginning on or about June 30, 1993. This project is a recompetition of the work being done under Contract No. N01-CM-07321 by Auckland UniService, Ltd., Auckland, New Zealand. (249) No collect calls will be accepted.

Copies of the RFP may be obtained by sending a written request to:

Ms. Bernice Evans  
National Cancer Institute  
Research Contracts Branch, TCS  
Executive Plaza South, Room 603  
Bethesda, MD 20892  
Telephone: (301) 496-8620

##### GENETIC AND MOLECULAR BASIS OF LONGEVITY

NIH GUIDE, Volume 21, Number 33, September 11, 1992

RFA AVAILABLE: AG-93-01:

P.T. 34; K.W. 1002019, 0710010, 0760015, 1002008, 0710030

National Institute on Aging



Letter of Intent Receipt Date: October 1, 1992  
Application Receipt Date: November 13, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute on Aging (NIA) invites applications for R01 grants to support basic research on the genetic and molecular bases of longevity. The goals of the Genetic and Molecular Basis of Longevity RFA are to identify genes that promote longevity and delay the onset of senescence, termed Longevity Assurance Genes (LAG), and determine the biochemical functions and molecular mechanisms of action of these LAGs. A multidisciplinary approach to these complex areas of basic research will facilitate the application of genetic, biochemical and molecular techniques to defining the genetic and molecular bases of longevity.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Genetic and Molecular Basis of Longevity, is related to the priority area of aging. Delineation of the genetic and molecular bases of longevity and senescence will lead to a fundamental understanding of aging processes and hasten the development of biological-based intervention strategies to extend the human health span. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-0325, telephone (202) 783-3238.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, research foundations, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from domestic institutions may include international components if the collaborative effort between domestic and foreign investigators strengthen the research application. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

The multidisciplinary, highly interactive approach outlined in this RFA is intended to facilitate and enhance research progress toward understanding complex problems in aging biology. This RFA is a one-time solicitation for research applications. The total project period for applications submitted in response to this RFA may not exceed five years. The anticipated award date for applications submitted in response to this RFA is July 1, 1993.

The Genetic and Molecular Basis of Longevity research program will be supported through the traditional research project grant (R01) mechanism. Applicants will be responsible for the planning, direction, and execution of the proposed research projects. Research applications from collaborating Principal Investigators at different institutions are highly encouraged if the combined expertise of the two research laboratories will facilitate the research progress of both laboratories and contribute to the overall research goals outlined in this RFA.

#### FUNDS AVAILABLE

The NIA will set aside a total of \$2,000,000 for funding research projects responsive to the Genetic and Molecular Basis of Longevity RFA in FY 1993 and expects to make eight to ten grant awards. Although this research initiative is provided for in the plans of the NIA, the award of research grants pursuant to this RFA is contingent upon the availability of appropriated funds in FY 1993 and the receipt of a sufficient number of responsive applications with high scientific merit.

#### RESEARCH OBJECTIVES

Research with several model systems including yeast, nematodes, drosophila, rats, mice, and cultured human cells has established that longevity and senescence are, in part, under genetic control. The purposes of this RFA are to stimulate research on the fundamental mechanisms of aging and senescence, to encourage the application of results obtained from model systems to understanding human longevity, and to develop intervention strategies to extend the human health span based on increased knowledge of fundamental aging mechanisms. The interactive, multidisciplinary approach outlined in this RFA is designed to focus the use of various model systems, human cells and cell lines, molecular reagents, and state-of-the-art molecular biology and biotechnology on this important area of aging biology. The development of sophisticated methods for molecular cloning, gene amplification, targeted gene insertion and disruption, and the production of germ-line transgenic organisms via molecular genetic manipulation of embryos or embryonic stem cells have made such an approach feasible. Application of these powerful molecular approaches to aging research will facilitate the identification of candidate LAG, allow evaluation of their effects on longevity and health span in transgenic model systems, and hasten the search for human homologs of key LAGs. It is anticipated that such an approach will facilitate and optimize research progress and hasten the development of biological-based intervention strategies designed to prevent or delay human aging processes and thereby extend the human health span.

The major objectives of the Genetic and Molecular Basis of Longevity RFA and research initiative are:

- o Development of molecular and animal resources to investigate the molecular basis of longevity;
- o Identification of candidate LAGs in appropriate models of aging;
- o Evaluation of candidate LAG effects on longevity and senescence in appropriate transgenic organisms;
- o Characterization of the regulation of LAG expression at the molecular level;
- o Characterization of the biological functions of proteins encoded by LAGs, and
- o Identification of human counterparts of key LAGs in cultured cells.

The development and application of several areas of molecular technology to these problems in aging biology have been identified as high priority including:

- o Development of suitable expression vectors and protocols for introduction and stable expression of targeted gene transplacements and the incorporation of multigenic DNA fragments in mouse embryonic stem cells.
- o Development of suitable expression vectors and protocols to achieve cell-specific expression of candidate transgenes in somatic cells of young adult and aged mice.
- o Identification and characterization of age-specific promoters and regulatory molecules that could be used to enhance the expression of candidate genes in aged organisms.
- o Identification of inducible promoters that will drive the expression of transgenes in aged and senescent animals.

The availability of additional animal models would aid in the identification and evaluation of candidate LAGs. For example, the creation of long-lived strains of mice by selective breeding of highly outbred founder populations and the genetic and molecular characterization of these strains is an important aspect of this research initiative. In addition, the creation and maintenance of transgenic mouse lines harboring key LAGs will provide another important animal resource for this and future research initiatives to define the genetic and molecular basis of longevity.

Several experimental strategies for the identification and evaluation of candidate LAGs appear to be appropriate for this RFA. These include the evaluation of the effects of known genes believed to have the characteristics of LAGs (for example, SOD, catalase, and LAG1) on longevity and health span in transgenic organisms, genetic mapping of candidate longevity loci in long-lived mouse strains, isolation and characterization of key genes (regulatory and structural) that are differentially expressed in animals subjected to caloric restriction compared to ad libitum fed controls, and identification of human homologs of LAGs using molecular probes isolated from other model systems. In addition, experiments to test the effect of candidate genes on longevity and senescence in transgenic organisms (invertebrate and vertebrate) is anticipated via targeted gene disruption and targeted gene transplacement are encouraged.

The research topics listed above should not be interpreted as the only experimental approaches to the identification of the genetic and molecular bases of longevity and senescence. Additional innovative approaches applicable to the research goals of this RFA are welcome and encouraged.

#### SPECIAL REQUIREMENTS

Applicants are responsible for proposing research projects that will advance the goals of the Genetic and Molecular Bases of Longevity research initiative. Applicants must have access to appropriate animal and/or cell culture models for aging research and have the necessary expertise in genetics, molecular biology, cell biology, or biochemistry to carry out the proposed research projects.

#### LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent by October 1, 1992. The letter of intent must include the number and title of this RFA (AG-93-01), a descriptive title of the proposed project, and the name, address, phone and FAX numbers of the Principal Investigator and key co-investigators. If the application will involve collaborative or consortium arrangements, the participating institutions must also be identified. Although a letter of intent is not binding and does not enter into the review of the subsequent application, the letter is requested to provide an indication to the NIA of the number and scope of applications to be reviewed.

Additional information related to the goals and scope of this RFA will be provided to investigators who have submitted a letter of intent. The letter of intent is to be addressed to:

Dr. Anna M. McCormick  
Biology of Aging Program  
National Institute on Aging  
Gateway Building, Suite 2C231  
Bethesda, MD 20892  
Telephone: (301) 496-6402  
FAX: (301) 402-0010

#### APPLICATION PROCEDURES

Applications are due November 13, 1992. The research grant application form PHS 398 (rev. 9/91) is to be used in applying for this grant. These forms are available from most institutional grants and business offices and from the Office of Grant Inquiries, Division of Research Grants, National Institutes of Health, Room 449,

Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892-4500.

#### REVIEW CONSIDERATIONS

Applications judged to be responsive to the RFA and competitive will be evaluated for scientific and technical merit by an appropriate ad hoc peer review group convened by the NIA Office of Scientific Review. The second level of review, which considers the priorities and special needs of the NIA, will be conducted by the National Advisory Council on Aging.

#### INQUIRIES

The program official welcomes the opportunity to clarify any issues or questions from potential applicants. Written and telephone inquiries concerning the objectives and scope of the Genetic and Molecular Basis of Longevity RFA, or whether a specific areas of research would be considered by the NIA as responsive to this RFA are encouraged.

Direct inquires regarding programmatic issues to:

Dr. Anna M. McCormick  
Chief, Biology Branch  
Biology of Aging Program  
National Institute on Aging  
Gateway Building, Suite 2C231  
Bethesda, MD 20892

Direct inquires regarding fiscal matters to:

Mr. Joseph Ellis  
Grants Management Officer  
Grants and Contracts Management Office  
National Institute on Aging  
Gateway Building, Suite 2N212  
Bethesda, MD 20892  
Telephone: (301) 496-1472

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic assistance No. 93.866. Awards are made under the authorization of the Public Health Service Act, Title IV, Part A (Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernment review requirements of Executive Order 12372 or Health Systems Agency review.

#### QUALITY OF LIFE ASSESSMENT IN SPECIAL POPULATIONS

NIH GUIDE, Volume 21, Number 33, September 11, 1992

RFA AVAILABLE: CA/NR-92-27

P.T. 34; K.W. 0730070, 0414014, 0413001, 0414013, 0785035

National Cancer Institute  
National Center for Nursing Research

Letter of Intent Receipt Date: October 23, 1992  
Application Receipt Date: January 19, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Cancer Institute (NCI) and the National Center for Nursing Research (NCNR) invite investigator-initiated grant applications (R01s) to develop methods for assessing health-related quality of life (QOL) or specific QOL dimensions in cancer patients from diverse sociocultural backgrounds.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Quality of Life Assessment in Special Populations, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, telephone 202-783-3238.



## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). The applicant has sole responsibility for planning, direction, and execution of the proposed project. Total project period for applications submitted in response to this RFA must not exceed three years.

This RFA is a one-time solicitation. Future unsolicited competitive continuation applications will compete with all other investigator-initiated research grant applications and be reviewed according to the customary NIH peer review procedures.

## FUNDS AVAILABLE

Total costs of \$1,600,000 per year for three years will be committed to specifically fund applications submitted in response to this RFA. It is anticipated that five to six awards will be made. This funding level is dependent upon the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI and the NCNR, the awards pursuant to this RFA are also contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

This RFA fosters development of methods for assessing health-related QOL in cancer patients from diverse sociocultural backgrounds. Objectives include: (1) development or adaptation of existing methods for use in culturally diverse populations; (2) validation of methods in the target population; and (3) pilot testing of methods in a clinical trial in the target population.

For this RFA, special populations include Hispanic Americans, Black Americans, low socioeconomic status groups, and persons with low literacy skills. Other smaller minority or ethnic groups such as Native Americans, may be considered under defined circumstances. Potential applicants are advised to contact NCI or NCRR program staff if there are any questions regarding the consideration of a particular research population.

Methods must focus on global health-related QOL or specific domains or aspects of QOL, such as functional status, physical symptoms, psychological function, and social function. Methods should evaluate within-person change over time. When feasible, adaptation of existing methodology for use in special populations is preferred.

General acceptability of the QOL assessment method must be evaluated in patients from the target population. Psychometric validation must include demonstration of reproducibility, construct validity, and responsiveness. Applicability must be demonstrated by pilot testing in a clinical research project.

## STUDY POPULATIONS

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without documentation will not be accepted for review.

## LETTER OF INTENT

Each prospective applicant is asked to submit, by October 23, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, telephone/FAX numbers of the Principal Investigator, the names of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, it contains information that is helpful in planning for the review. It allows NCI and NCNR staff to estimate the potential review workload and to avoid possible conflict of interest in the review. The letter of intent is to be sent to the Program Director named in INQUIRIES.

## APPLICATION PROCEDURES

Applications must be received by January 19, 1993. Application form PHS 398 and information about application procedures may be obtained from the NCI Program Director named in INQUIRIES.

## REVIEW CONSIDERATIONS

Applications that are competitive and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group according to specific review criteria. A second level of review will consider special needs and research priorities of the NCI and the NCNR.



## INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome. Direct requests for the RFA and inquiries regarding programmatic issues to:

Susan G. Nayfield, M.D., M.Sc.  
National Cancer Institute  
Executive Plaza North, Suite 300  
Bethesda, MD 20892  
Telephone: (301) 496-8541

Direct inquiries regarding fiscal matters to:

Mrs. Eileen M. Natoli  
National Cancer Institute  
Executive Plaza South, Suite 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.399, Cancer Control Research, and 93.361, Nursing Research. Awards are made under the authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ERRATUM

### CAREER DEVELOPMENT AWARDS FOR UNDERREPRESENTED MINORITY CLINICIAN-INVESTIGATORS

NIH GUIDE, Volume 21, Number 33, September 11, 1992

RFA: DK-93-03

P.T. 34, FF; K.W. 0785035, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases

The following paragraphs are to be added under the appropriate sections to the Request for Applications DK-93-03 that was published in the NIH Guide for Grants and Contracts, Vol. 21, No. 31, August 28, 1992.

### ELIGIBILITY REQUIREMENTS

For the purposes of this announcement, underrepresented minority investigators are individuals belonging to a particular racial or ethnic group that has been determined by the grantee institution to be underrepresented in biomedical or behavioral research. Nationally, individuals who have been found to be underrepresented in biomedical or behavioral research include, but are not limited to, Black Americans, Hispanic Americans, Native Americans, and Pacific Islanders.

### MECHANISMS OF SUPPORT

Grant funds awarded under the CIA and the PSA mechanisms are for the development of research training only and may not be used for the support of clinical training or clinical services. Such activities must be supported from other funding sources.

## INQUIRIES

Direct requests and inquiries regarding programmatic issues to:

Lois F. Lipsett, Ph.D.  
Division of Diabetes, Endocrinology, and Metabolic Diseases  
Telephone: (301) 496-7433

### WORKSHOP ON MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

NIH GUIDE, Volume 21, Number 33, September 11, 1992

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The correct telephone number for inquiries regarding the Workshop on Minimizing Pain and Distress in Laboratory Animals co-sponsored by the National Institutes of Health, Vanderbilt University, and Meharry Medical College, on December 3 - 4, 1992, is (615) 322-4030. The telephone number given in the NIH Guide for Grants and Contracts, Vol. 21, No. 31, August 28, 1992 was incorrect.

INQUIRIES

For information regarding future workshops, contact:

Ms. Roberta Sonneborn  
Telephone: (301) 496-7163  
FAX: (301) 402-2803



**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

**5333 Westbard Avenue  
Bethesda, MD 20816**

**THE NIH GUIDE WILL NOT BE PUBLISHED ON SEPTEMBER 18, 1992. THE NEXT ISSUE OF THE GUIDE WILL BE SEPTEMBER 25, 1992.**

# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 34, Part I of II  
September 25, 1992

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES

SUPPORT OF PROGRAM PROJECT GRANTS

NIH GUIDE, Volume 21, Number 34, September 25, 1992

P.T. 34; K.W. 1014006, 0710030

National Institute of General Medical Sciences

PURPOSE

This announcement updates and summarizes the policy of the National Institute of General Medical Sciences (NIGMS) regarding program project grants (P01). IT IS NOT AN ANNOUNCEMENT OF ANY NEW PROGRAM OR INITIATIVE. Rather, it represents a clarification of existing policies. Since many investigators have inquired about the intent and purposes of NIGMS-supported program project grants and their relationships to other support mechanisms, the following description and summary is intended to be helpful to potential applicants.

The NIGMS supports research in the areas of Cellular and Molecular Basis of Disease, Genetics, Pharmacological Sciences, and Biophysics and Physiological Sciences. Program project grants are investigator-initiated, but because of budgetary constraints may be restricted to areas of special interest to the individual programs within the NIGMS. Potential applicants are advised to contact the NIGMS program staff listed at the end of this announcement for guidance in the areas appropriate for program project grant applications and the preparation of the application itself.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government.

RESEARCH OBJECTIVES

The program project mechanism is designed to support research in which the funding of several projects as a group offers significant scientific advantages over support of these same projects as individual research grants. Successful program projects generally bring together scientists in diverse fields, who might not otherwise collaborate, to work on a well-defined problem or goal. As a result, an environment for interdisciplinary research is created. In addition, the program project can facilitate the support of essential shared core facilities, e.g., major equipment, although the need of a group of investigators for a major piece of equipment or a core facility does not in itself provide sufficient justification for a program project grant.

Usually, a program project consists of three to five individual projects. The scientist designated by the applicant institution as the Principal Investigator bears responsibility for the overall scientific leadership and fiscal management of the program project grant. It is expected that each of the collaborating scientists responsible for the individual projects will be independent investigators. Investigators from more than one department, administrative unit, or institution (through a sub-contract mechanism) are commonly included.

The program project grant is not intended to be a vehicle for departmental support, nor is the research support



of one senior investigator and several postdoctoral and research associate-level scientists appropriate under this mechanism. In addition, the program project and each individual project must represent a significant effort on the part of the participating scientists and should be distinct from their other funded efforts. If individuals have substantial support in areas closely related to the program project and cannot fold this support into the program project, they may participate as associate members. Associate members have full use of, for example, core facilities, and contribute to the overall collegiality of the project, but derive no financial support from it.

#### APPLICATION PROCEDURES

There is an upper limit to the budget that may be requested in a competing program project grant application to the National Institute of General Medical Sciences. This limit (exclusive of subcontractual indirect costs) over a five-year period is given in the table below:

	Direct Costs	Receipt Date
FY 93	\$ 3,600,000	February 1, 1992 and later
FY 94	\$ 3,750,000	February 1, 1993 and later
FY 95	\$ 3,900,000	February 1, 1994 and later
FY 96	\$ 4,000,000	February 1, 1995 and later

Under certain circumstances, additional funds may be provided for major pieces of equipment.

Because individual programs have different scientific and budgetary priorities, applicants are urged to consult NIGMS staff prior to submission of a program project grant application. Requests for details of research areas supported by the NIGMS and inquiries exploring the suitability of the program project grant mechanism may be directed to the program staff listed at the end of this announcement.

Applications are to be prepared using form PHS 398 (rev. 9/91 and available at most institutional business offices and from the Division of Research Grants, NIH) and the additional guidelines stated below. The receipt dates for new and renewal program project grant applications are February 1, June 1, and October 1. The earliest possible award dates will be approximately nine months after the receipt dates. Applications received too late for one cycle of review will be held for the next.

The program project grant application is to be structured as a series of separate but related project proposals. The following format is to be used:

Overall Proposal: An introductory section must contain justification for the program project grant mechanism and describe those goals that are not readily attainable through individual research project grants. This section must include:

- o a face page;
- o an abstract;
- o a description of the objectives of the program as a whole, the relationship of the individual research projects to the entire program project, and the special benefits to be achieved by funding as a program project grant rather than as a series of individual research grants;
- o a list of participating personnel;
- o the consolidated budget for the program project grant (summarizing budgets for the component parts and core);
- o a description of facilities available, including major instruments and special program resources;
- o administrative arrangements for overall scientific leadership, quality control, and management of the program project grant; and
- o a separate, overall listing of the proposed percent effort on the program project grant and actual and pending research support from all sources for each participating investigator (including percent effort devoted to each project). This section must also detail the relationship of existing support to the proposed program project and describe planned modification to that support in the event of funding, for example, folding in support for related funded research.

Component Projects: Each individual project of a program project grant must represent an independent as well as an interdependent research effort, and must be prepared in the format of an individual research grant application. The face page, abstract, budget pages, biographical information, a detailed description of the research to be conducted, and any justification for human and animal experimentation, if applicable, must be included. If support of core resources is requested, a separate component describing and justifying these must be included.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

## REVIEW CONSIDERATIONS

Program project grant applications are reviewed by either the Division of Research Grants or the NIGMS Office of Review Activities, depending on the subject. The applicant should not assume that a site visit will accompany the review of a program project grant application. Therefore, the application must be sufficiently complete so that it can be reviewed without a site visit.

The individual projects within a program project grant, as well as the program project grant as a whole, must meet the same standards of scientific merit as those required of individual research project grants. The scientific merit of the entire program project grant application, as well as its coherence as a program, will be assessed. In addition, the scientific merit of each individual project will be assessed and a priority score assigned. This assessment will be based both on the scientific merit of the individual project as an independent effort and on its potential importance to the success of the total effort.

## AWARD CRITERIA

Final review and recommendations by the National Advisory General Medical Sciences Council will take into account the scientific merit of both the individual projects and the program project as a whole. It is possible that funding for some of the individual projects or core components favorably recommended by the initial review group may be deleted by Council or by NIGMS staff prior to award of a grant, based on the scientific merit of these components or the lack of coherence with the rest of the program project. The Council will also judge the appropriateness of the application to the mission of the programs within the NIGMS, taking into account the budgetary situation at the time of funding. In addition, the total support of the Principal Investigator, the group of investigators as a whole, or any individual investigator may be considered in funding the entire program project or any part thereof.

## INQUIRIES

For further information, applicants are advised to contact the NIGMS program staff listed below:

Biophysics and Physiological Sciences:	Dr. James Cassatt, (301) 496-7463
Trauma and Burn Injury Research:	Dr. Lee Van Lenten, (301) 496-7001
Cellular and Molecular Basis of Disease:	Dr. Bert I. Shapiro, (301) 496-7518
Genetics:	Dr. Judith Greenberg, (301) 496-7175
Pharmacological Sciences:	Dr. Christine Carrico, (301) 496-7707
Anesthesiology:	Dr. Alison Cole (301) 496-7707
Biorelated Chemistry:	Dr. Michael Rogers, (301) 496-7181

All correspondence may be addressed to:

National Institute of General Medical Sciences  
Westwood Building  
5333 Westbard Avenue  
Bethesda MD 20892

For general information, applicants may contact Dr. W. Sue Shafer, (301) 496-7061 and for business management aspects, Ms. Carol Tippiery, (301) 496-7746.

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.862, 93.821, 93.863, and 93.859. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## WORKSHOP ON MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

NIH GUIDE, Volume 21, Number 34, September 25, 1992

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health, (NIH), Office for Protection from Research Risks (OPRR), is continuing to sponsor workshops on implementing the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Each of the workshops scheduled for FY 1993 will focus on a specific theme.

The workshops are open to institutional administrators, members of Institutional Animal Care and Use Committees, laboratory animal veterinarians, investigators and other institutional staff who have responsibility for high-quality management of sound institutional animal care and use programs.

DATE: December 3-4, 1992

TOPIC: MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

LOCATION:  
Loews Vanderbilt Plaza Hotel  
2100 West End Avenue  
Nashville, TN 37203

Telephone: (615) 320-1700  
FAX: (615) 320-5019

**SPONSORS:**

Vanderbilt University  
Meharry Medical College

**REGISTRATION:**

Vanderbilt Division of Continuing Medical Education  
D-8211 Medical Center North  
Nashville, TN 37232-2337  
Telephone: (615) 322-4030

**DATE:** June 10-11, 1993

**TOPIC:** REGULATORY AND ETHICAL RESPONSIBILITIES: THE ANIMAL UNIT; THE INSTITUTIONAL ADMINISTRATORS; THE IACUC

**LOCATION:**

Oklahoma City Marriott  
3233 Northwest Expressway  
Oklahoma City, OK 73112  
Telephone: (405) 842-6633  
FAX: (405) 842-3152

**SPONSOR:**

The University of Oklahoma College of Medicine

**REGISTRATION:**

Ms. Marilyn Perry, Assistant to Director for Compliance  
Division of Animal Resources  
BMSB/Room 203  
The University of Oklahoma Health Sciences Center  
Oklahoma City, OK 73190  
Telephone: (405) 271-5185  
FAX: (405) 271-3032

**NATIONAL HUMAN SUBJECT PROTECTIONS WORKSHOPS**

**NIH GUIDE**, Volume 21, Number 34, September 25, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The Office for Protection from Research Risks (OPRR) of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

**SOUTHWESTERN WORKSHOP**

**DATES:** November 16 & 17, 1992

**LOCATION:**

Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

**SPONSORS:**

University of Texas Health Science Center at Houston  
Prairie View A & M University

**REGISTRATION:**

Ms. Paula Knudson, Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

**TITLE:** Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

**DESCRIPTION:** Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key

problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, other health care professionals, clergy, lawyers, medical, nursing, social work students, and psychologists as well as IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

#### SOUTHEASTERN WORKSHOP

DATES: January 14 & 15, 1993

#### LOCATION:

Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

#### SPONSORS:

University of South Florida  
Florida A & M University

#### REGISTRATION:

Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Issues such as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

#### SOUTHWESTERN WORKSHOP

DATES: February 12 & 13, 1993

#### LOCATION:

Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

#### SPONSORS:

Arizona State University  
Northern Arizona University

#### REGISTRATION:

Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

TITLE: Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

DESCRIPTION: This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.



This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. IRB members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

For further information regarding these workshop or future NIH/FDA National Human Subject Protections Workshops, contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

##### DIABETES IN NATIVE AMERICANS AND ALASKA NATIVES

NIH GUIDE, Volume 21, Number 34, September 25, 1992

RFA AVAILABLE: DK-92-17

P.T. 34, FA, FE; K.W. 0715075

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: November 12, 1992  
Application Receipt Date: December 8, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

This RFA invites new and experienced investigators to submit clinical research applications designed to develop and validate intervention approaches to the amelioration or prevention of diabetes mellitus and/or its complications among American Indians and Alaska Natives. This RFA is a follow-up to the RFA (DK-91-01) Collaborative Research Planning Grant-Diabetes in American Indians and Alaska Natives. However, respondents to this RFA are not restricted to those having previously received a planning grant under the prior RFA.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Diabetes in Native Americans and Alaska Natives, is specifically targeted at diabetes mellitus and its complications as a major public health problem. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, non-profit and for-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments and eligible agencies of the Federal government. Teams of applicants are encouraged, which could include universities, public health departments, Indian Health Service (IHS) hospitals, voluntary organizations, health clinics, and Federally recognized Indian tribe or tribal organizations as defined in P.L. 93-638 and amended by P.L. 100-472, or combinations thereof. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

The support mechanism for this research will be the individual research grant (R01) and the First Independent Research Support and Transition (FIRST) Award (R29). This is a one-time solicitation. Subsequent unsolicited competing continuation applications will compete with all investigator-initiated applications and will be reviewed according to customary peer review procedures. This RFA will provide the opportunity for investigators to establish support for periods up to five years for meritorious research projects designed to develop and validate intervention approaches to the amelioration or prevention of diabetes mellitus and/or its complications among American Indians and Alaska Natives.

Foreign institutions are not eligible for FIRST awards.

#### FUNDS AVAILABLE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) plans to support approximately eight to ten applications submitted in response to this solicitation and \$2 million total costs (direct and indirect costs) for this program have been included in the financial plans for fiscal year 1993. The number of awards to be made is dependent upon receipt of a sufficient number of applications of high scientific merit and upon availability of funds. Although this program is provided for in the financial plans of the NIDDK, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

Diabetes mellitus and its complications are major public health problems in the United States today. The National Institutes of Health (NIH) has encouraged research into the cause, cure, and prevention of diabetes and its related endocrinologic and metabolic disorders. The Report of the Secretary of Health and Human Services Task Force on Blacks and Minority Health (1) identified non-insulin dependent diabetes mellitus (NIDDM) and its complications as major public health problems in several minority populations. In the U.S., the rates of NIDDM are often two to five times higher among American Indians than among the general U.S. population. For example, population based surveys have shown that the incidence of diabetes in the Pima Indians of Arizona is 19 times greater than in Caucasians of Rochester, Minnesota, and the difference continues to increase with time. A partial explanation of this disproportionate occurrence may be related to obesity. It is well established that obesity is a major risk factor for NIDDM, and certain Indian populations have a much higher prevalence of obesity than the majority of the U.S. population.

The overall objective of this RFA is to stimulate original and innovative studies directed at the elucidation of practical methods for the reduction of the public health burden of diabetes in Native American and Alaska Native populations.

Examples of possible research topics relevant to this RFA include, but are not limited to:

- o Development and validation of interventions designed to prevent NIDDM or its major risk factors, such as obesity on a community wide basis.
- o Development and validation of interventions designed to prevent NIDDM in targeted high risk subgroups (e.g., documented impaired glucose tolerance, history of gestational diabetes, obese children or young adults) within the population.
- o Development and validation of interventions designed to improve the care of patients with NIDDM.
- o Development and validation of interventions designed to reduce or prevent the long-term complications of diabetes among those with the disease.
- o Clinical studies of the physiologic effects of alternative pharmacologic and non-pharmacologic interventions for the treatment of NIDDM.

## STUDY POPULATIONS

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS.

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of women in studies of diseases, disorder and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

## LETTER OF INTENT

Prospective applicants are asked to submit, by November 12, 1992, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of key personnel, the participating institutions, and the number and title of the RFA to which the applicant is responding. Such letters are requested for the purpose of obtaining an indication of the number and scope of applications to be received. The letter is not binding, is not a requirement for submission, and does not enter into the review of the application.

The letter of intent is to be sent to:

Robert Hammond, Ph.D.  
Chief, Review Branch  
National Institute of Diabetes and Digestive and Kidney Disorders  
Westwood Building, Room 605  
Bethesda, MD 20892  
FAX: (301) 402-1277

## APPLICATION PROCEDURES

The research grant application form PHS-398 (rev. 9/91) is to be used. This form is available from the institutional offices of sponsored research, and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441.

## REVIEW CONSIDERATIONS

Applications that are not responsive to the research goals and scope of this RFA will be returned to the investigator. If the number of applications is large compared to the number of awards to be made, the NIDDK may conduct a preliminary scientific peer review (triage) to eliminate those applications that are clearly not competitive. Those applications will be withdrawn from further review and the applicant and institutional business office will be notified. Responsive applications received in response to this RFA will first be

reviewed for scientific and technical merit by an Initial Review Group convened by the Review Branch, Division of Extramural Program Activities, NIDDK. A secondary review for policy and program relevance to the NIDDK mission will be made by the National Diabetes and Digestive and Kidney Diseases Advisory Council.

#### INQUIRIES

It is imperative that prospective applicants obtain the RFA before developing their applications. Also, the opportunity to clarify any issues or questions from potential applicants is welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Charles A. Wells, Ph.D.  
Diabetes Research Program Director  
Division of Diabetes, Endocrinology and Metabolic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 622  
Bethesda, MD 20892  
Telephone: (301) 402-2599

Direct inquiries regarding fiscal matters to:

Betty E. Bailey  
Grants Management Specialist  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.847, Diabetes Endocrinology and Metabolism Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78- 410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### DIETARY PATTERNS AND BLOOD PRESSURE

NIH GUIDE, Volume 21, Number 34, September 25, 1992

RFA AVAILABLE: HL-92-11-P

P.T. 34; K.W. 0710095, 0715115, 0755015

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: November 1, 1992  
Application Receipt Date: December 1, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

#### PURPOSE

The Division of Epidemiology and Clinical Applications (DECA) invites cooperative agreement applications for an estimated four Field Centers and one Coordinating Center to participate, along with the assistance of the National Heart, Lung, and Blood Institute (NHLBI), in a collaborative multicenter clinical trial on dietary patterns and blood pressure. The solicitation is for three years, six months for Field Centers and four years for the Coordinating Center.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Dietary Patterns and Blood Pressure, is related to the priority areas of heart disease and stroke, and nutrition. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign organizations are not eligible to apply and domestic applications may not include international components. Applications from minority individuals and women are encouraged.



## MECHANISM OF SUPPORT

The administrative and funding mechanism to be used to undertake this program will be a cooperative agreement (U01), an assistance mechanism. Under the cooperative agreement, the NIH assists, supports, and/or stimulates and is substantially involved with recipients in conducting a study by facilitating performance of the effort in a "partner" role.

## FUNDS AVAILABLE

An estimated four awards for Field Centers and one award for a Coordinating Center will be made under this RFA. A maximum of \$6.9 million (including direct and indirect costs) over a four-year period will be awarded for Field Centers and the Coordinating Center with at least two-thirds apportioned to the Field Centers. Approximately \$1.65 million will be available for the first year, \$2.55 million for the second year, \$1.90 million for the third year, and \$0.8 million for the last year. This will be allocated among the four Field Centers and the Coordinating Center.

## RESEARCH OBJECTIVES

The strong relationship between diet and blood pressure and the risk of hypertension was described in detail in Diet and Health (National Research Council, 1989), a comprehensive review of epidemiologic, clinical, and laboratory research prepared by the Committee on Diet and Health of the National Research Council. Currently, only three specific diet-related factors have been recommended by the Joint National Committee on High Blood Pressure as a first-line approach in treating mild hypertension: caloric restriction for weight reduction, reduced consumption of alcohol, and lower sodium intake. Many studies, primarily observational, have shown significant associations between blood pressure and diet-related factors other than weight, alcohol, and sodium. Because of the potential of macronutrients and micronutrients to play an important role in reducing blood pressure, this RFA requests investigators to propose testing dietary patterns that are likely to lower blood pressure.

This study will test the effect of dietary patterns on blood pressure by means of a randomized, controlled clinical trial. To ensure good compliance with the experimental diets, food comprising the dietary patterns will be provided to the participants.

The study design will be a randomized, controlled clinical trial testing the effect of dietary patterns on blood pressure. The effects on blood pressure of alcohol, sodium, and weight, or a vegetarian dietary pattern per se are outside the scope of this RFA.

The study population is envisioned to be adults with high normal blood pressure or with mild hypertension, in order to be more likely to detect an effect, if present, than in those with completely normal blood pressure.

The overall population to be studied should provide data that are broadly applicable to diverse minority groups as well as whites; thus, the composition of the study population in this RFA program must reflect this diversity. Because of the enormity of the problem of hypertension in the African American population, at least one Center that will recruit predominantly (90 percent or more) African Americans will be selected. It is expected that the other three centers will recruit over 50 percent minorities.

The timetable for the study may be loosely subdivided into three phases covering about a three and one half to four year period. Phase I consists of the first six to nine months of study and may be devoted to planning and protocol development. In Phase II, subject recruitment and protocol implementation are estimated to proceed over a 24-month period. Phase III will consist of study closeout by Field Centers (estimated six to nine months) and the Coordinating Center (estimated 12 months).

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by November 1, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NHLBI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

C. James Scheirer, Ph.D.  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 648  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7363  
FAX: (301) 402-1660



## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441; and from the NIH Project Scientist named below.

Applications must be received by December 1, 1992. An application received after this date will be considered ineligible.

## REVIEW CONSIDERATIONS

Applicants are encouraged to submit and describe their own ideas on how best to meet the goals of the study, but they are expected to address issues identified under SPECIAL REQUIREMENTS of the RFA. NOTE THAT THIS DOCUMENT IS NOT THE RFA. Applications will be judged primarily on the scientific quality of the application, the availability of a study sample with adequate numbers of participants, evidence of ability to prepare and deliver food to participants, the discussion of considerations relevant to this RFA, expertise of the investigators, their capability to perform the work proposed, and a demonstrated willingness to work together with other Centers and the NHLBI Project Scientist.

The review group will assess (as further detailed in the RFA):

### Field Centers

- o Scientific merit of the study.
- o Plans to recruit participants and plans delineating the feasibility and logistics of providing food to participants.
- o Qualifications, experience, and commitment of key personnel.
- o Facilities, equipment, and organizational structure to effectively implement the proposed research.
- o Appropriateness of the budget for the work proposed.

### Coordinating Center

- o Scientific merit of the study.
- o Organizational, administrative, and supervisory ability and statistical expertise to serve as a Coordinating Center for a multicenter randomized controlled feeding trial.
- o Qualifications, experience, and commitment of key personnel.
- o Facilities and equipment to function as a Coordinating Center for a multicenter trial.
- o Appropriateness of the budget for the work proposed.

## AWARD CRITERIA

Applications recommended by the National Heart, Lung, and Blood Advisory Council will be considered for award based upon (a) scientific and technical merit and the requirements explicitly stated in this RFA, (b) program balance, including in this instance, sufficient compatibility of features to make a successful collaborative program a reasonable likelihood, and (c) availability of funds.

Letter of Intent	November 1, 1992
Application Receipt Date	December 1, 1992
Review by National Heart, Lung, and Blood Advisory Council:	May 1993
Anticipated Award Date	July 1, 1993

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Inquiries regarding this announcement and requests for the RFA may be directed to:

Eva Obarzanek, Ph.D., R.D.  
Prevention and Demonstration Research Branch  
Division of Epidemiology and Clinical Applications  
National Heart, Lung, and Blood Institute  
Federal Building, Room 604  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-2465

Inquiries regarding fiscal and administrative matters may be directed to:

Mr. William W. Darby  
Section Chief, Grants Management Office  
Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A11C  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7536



3 1496 00537 2415

#### AUTHORITY AND REGULATIONS

This project is described in the Catalog of Federal Domestic Assistance No. 93.837. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR 74. This project is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 34, Part II of II  
September 25, 1992

RICHARD W HURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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ONGOING PROGRAM ANNOUNCEMENTS

MINORITY MENTAL HEALTH RESEARCH CENTERS

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA AVAILABLE: PA-92-104

P.T. 04, FF; K.W. 0715095, 0715129, 0710030

National Institute of Mental Health

THE PROGRAM ANNOUNCEMENT (PA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE PROGRAM ANNOUNCEMENT FROM THE CONTACT NAMED IN "INQUIRIES" BELOW.

PURPOSE

The National Institute of Mental Health (NIMH) provides support for the development, conduct, and maintenance of Minority Mental Health Research Centers (MMHRCs) both to stimulate and enable research that could not be done without the particular facilities and environment that such centers provide. MMHRCs should provide stimulating and productive research environments in which experienced and junior mental health researchers can interact and direct their energies toward the conceptualization, development, and conduct of coordinated, multidisciplinary research on mental health issues related to minority populations. All research areas supported by NIMH are relevant to the mental health of minority populations and are appropriate as central foci for center research.

The specific minority populations that the NIMH will award grants to study include: American Indians/Alaskan Natives, Asian Americans, African Americans, Hispanics, and Native Hawaiians/Pacific Islanders.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Minority Mental Health Research Centers, is related to the priority area of mental health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: 202/783-3238).

ELIGIBILITY REQUIREMENTS

Eligible applicant institutions include any domestic non-profit or for-profit organization that is a doctorate-granting institution and has an established relevant research capacity or is an organization with a documented affiliation with such an institution.



## MECHANISM OF SUPPORT

Research center support may be requested only through applications for a regular research grant (R01).

## RESEARCH OBJECTIVES

The principal objective of all NIMH-supported MMHRCs is to provide a research environment, in which state-of-the-art research methodologies may be applied to issues relating to the understanding and improvement of mental health and the prevention and treatment of mental illness of the specific minority group(s) selected for the focus of the MMHRC. Each MMHRC must provide an environment of scientific excellence that will assure the highest quality research and leadership in its particular area(s) of investigation. Through its activities, the MMHRC should already be, or demonstrate that it has the potential to become, a major national scientific research resource.

Models for MMHRCs may vary, but they should all contain the infrastructure for implementing an overarching research plan, a plan that includes sophisticated, multidisciplinary, integrated research projects. The MMHRC should enable investigators to conduct both pilot and comprehensive studies and to formulate, develop, and test new methodologies and data-gathering techniques. The infrastructure of each MMHRC must include, at minimum, the following elements:

**Administrative Core:** a strong administrative structure, including a scientifically and administratively well-qualified director with primary responsibility for scientific leadership and administration of the research program.

**Methodology and Statistics Core:** on-site expertise in research design methodology, data-base management, and statistical analysis.

Applicants must describe in detail the Administrative Core, including the research program management structure of the MMHRC, and the Methodology and Statistics Core. The research plan should describe the overarching research focus for the MMHRC. The plan should be based on a set of integrated research areas related to the overarching focus. The research plan should describe how each research area and the individual research projects within each are linked to the central focus of the MMHRC. Applicants must also describe the types of further programmatic steps that might be taken in future years to build upon early findings. In addition, a statement describing relevant current and planned research, training, and service grant support that will be available to the MMHRC should be included.

Each research area should include several developmental projects, pilot studies, and exploratory/feasibility studies. Separate descriptions must be provided for each major research area, including summary descriptions of individual developmental research projects to be supported in each area and how these projects will relate to and support each other.

Budgets for the MMHRC Administrative Core, Methodology and Statistics Core, research areas, and individual research projects must be presented in aggregate and separately and must be fully justified.

The following elements must be specifically addressed in each application:

- o An MMHRC will focus, in general, on hypothesis testing, methodological development, feasibility studies, and pilot studies in its initial years. Early phases of major studies can be supported by the MMHRCs initial grant.

- o The primary purpose of a Center is to carry out research. It is expected that research projects will be developed in ensuing years with support from separate research and research training grants from the NIMH and other research grant awarding sectors of the Federal government and from private foundations. However, initial applicants are not expected to have extensive additional research funding.

- o Funds from the MMHRC grant may not be used to support formal research training activities. However, each MMHRC should include a plan for providing opportunities for research training experiences in disciplines relevant to mental health.

- o An MMHRC should establish, when appropriate to the central focus of the research, a collaborative relationship with public facilities where severely mentally ill patients are cared for on both inpatient and outpatient basis.

- o An MMHRC must have the following: (a) strong intellectual leadership; (b) the availability of mental health researchers, especially members of the minority group(s) who have experience in mental health-relevant research for that minority group; and (c) the availability of promising junior researchers who are either graduate students or junior faculty.

- o An MMHRC must be multidisciplinary, including, as appropriate, researchers from neuroscience, molecular biology, genetics, health economics, sociology, public health, epidemiology, psychiatry, nursing, social work, psychology, statistics, and demography.

- o An MMHRC must include a central conceptual focus for the research and involve strong, collaborative, synergistic relationships among the researchers, that will form the basis for further research and research training activities. All activities must be interrelated to reflect an integrative MMHRC rather than an uncoordinated or loosely allied network of researchers.

- o An MMHRC must have access to the target minority groups or subgroups in sufficient numbers to accomplish its goals.

- o An MMHRC must have an administrative structure headed by the Principal Investigator/MMHRC Director that will ensure maximum effectiveness and efficiency of operation and sound financial practices, and facilitate coordination among center personnel.

- o An MMHRC must have a Principal Investigator, who serves as Director of the MMHRC, providing scientific leadership by devoting no less than 60 percent of his/her time to the Center, including time spent on Center research projects.

- o The MMHRC Director is responsible for the planning and coordination of the Center program, preparation of the budget, control of expenditures, staff appointments, and space allocation. However, the day-to-day management and the

responsibility for the administrative and operational aspect of the MMHRC may be delegated.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

Applicants are to use the research grant application form PHS 398 (rev. 9/91). The number and title of this announcement, Minority Mental Health Research Centers, PA-92-104, must be typed in item number 2a on the face page of the PHS 398 application form.

Applications for an MMHRC grant must include: (1) an overall organizational plan, (2) an overarching research plan, and (3) detailed plans for the research areas and individual research projects. For purposes of the page limitations of sections 1 through 4 of form PHS 398, the MMHRC organizational plan (including the Administrative Core and the Methodology and Statistics Core) and the overarching research plan are to be considered one component with a 25-page limit. A maximum of 25 additional pages may be used for each research area that the Center will address.

Application kits containing the necessary forms may be obtained from business offices or offices of sponsored research at most universities, colleges, medical schools, and other major research facilities, and from the Grants Management Branch, National Institute of Mental Health, 5600 Fishers Lane, Room 7C-05, Rockville, MD 20857, telephone: 301/443-4414.

The signed original and five legible copies of the completed application must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications for all MMHRCs will be reviewed for scientific and technical merit by an initial review group (IRG) composed primarily of non-Federal scientific experts. Final review is by the appropriate National Advisory Council; review by Council may be based on policy considerations as well as scientific merit. By law, only applications recommended for consideration for funding by the Council may be supported. Summaries of IRG recommendations are sent to applicants as soon as possible following IRG review.

Criteria to be considered in evaluating applications for scientific/technical merit include:

- o Scientific, technical, or medical significance and originality of the proposed research
- o Appropriateness and adequacy of the research approach and methodology proposed to carry out the research
- o Qualifications and research experience of the Principal Investigators and staff, particularly but not exclusively in the area of the proposed research
- o Availability of resources necessary to the research
- o Appropriateness of the proposed budget and duration in relation to the proposed research
- o Adequacy of the proposed means for protecting against or minimizing adverse effects to human and/or animal subjects

#### AWARD CRITERIA

The decision to fund applications will be based on a consideration of the following criteria:

- o Scientific merit and quality of the proposed MMHRC as determined during the review process
- o Availability of funds
- o Geographic distribution of MMHRCs
- o Program balance

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Delores Parron, Ph.D.  
Associate Director for Special Populations  
National Institute of Mental Health  
5600 Fishers Lane, Room 17C-16  
Rockville, MD 20857  
Telephone: (301) 443-2847

Direct inquiries regarding fiscal matters to:

Stephen J. Hudak  
Chief, Grants Management Section  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C-23  
Rockville, MD 20857  
Telephone: (301) 443-4456

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.242, Mental Health Research Grants. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This announcement is not subject to the intergovernmental review requirements of Executive Order 12372, as implemented through DHHS regulations at 45 CFR Part 100, or Health Systems Agency review.

#### WOMEN'S HEALTH OVER THE LIFECOURSE: SOCIAL AND BEHAVIORAL ASPECTS

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA NUMBER: PA-92-105

P.T. 34, FF, II; K.W. 0745035, 0404000, 0417000

National Institute on Aging  
National Institute of Child Health and Human Development  
National Institute of Mental Health

#### PURPOSE

The National Institute on Aging (NIA), the National Institute of Child Health and Human Development (NICHD), and the National Institute of Mental Health (NIMH) invite qualified researchers to submit applications for research to investigate social and behavioral aspects of women's health during adulthood. Research is needed to understand the natural course and consequence of the aging processes of women (e.g., healthy life expectancy) in a general population of reproductive-aged, middle aged and older women, as well as a wide range of special women's issues (i.e., health related behaviors, family life, role and task demands, psychological well-being, work and productivity) that may be related to health and/or aging. Special emphasis on minority women is an integral part of this solicitation.

Differences between men and women in health and illness, mortality and social circumstances, appear across the adult lifecourse. Women constitute about 60 percent of the population aged 65 and over and approximately 70 percent of those 85 and over (Lamphere-Thorpe & Blenden, 1991). While they live longer, women also experience more chronic illness and disability than men, due to higher incidence of nonfatal chronic conditions, such as rheumatoid arthritis, depression, and osteoporosis (Ory and Warner, 1990). More than half of women 75 and over live alone. Of those older women who live alone, they are five times more likely to be living in poverty as compared to men of the same age (Aging America, 1991).

There are differences in the circumstances of younger and midlife women from those of older women. Women born in 1940 or later experience later onset of childbearing, fewer children, and complete families sooner than women born 1910-1940. These women experience higher divorce rates and are less likely to have children than women from older cohorts (U.S. Bureau of the Census, 1990). Younger and midlife women may be particularly likely to be balancing competing demands of differing role responsibilities.

The lifecourse of women, including the timing of family formation and child-rearing, and aging, is affected by differences in their experiences. Family situations and work patterns, including labor force participation and child-rearing, help shape the character of other experiences of women, including reproduction, menopause and aging. Conversely, the order and timing of lifecourse events, in addition to chronological age, may also determine family situations and work experiences. Women's situations are further influenced by ethnicity and cultural practices, neighborhood environments, living arrangements and socioeconomic status. Health and illness may influence, as well as be influenced by, these aspects of women's lives.

This Program Announcement (PA) supplements, but does not replace earlier PAs on related topics (see NIH Guide for Grants and Contracts Vol. 17, No. 18, May 20, 1981: Gender and Aging: Relation To Health and Longevity, and NIH Guide for Grants and Contracts, Vol. 20, No. 36, September 27, 1991: Special Issues in Women's Health Over the Life Cycle).

The NIA has a particular interest in supporting research on the health and well-being of middle-aged and older women. Earlier social and behavioral research efforts have included studies of women's health and functioning in mid-life, gender differences in specific chronic conditions (e.g., arthritis), burdens of caregiving, family relationships and widowhood, and women's perceptions and responses to normal aging (e.g., menopause).

The NICHD is concerned with the health of women during the reproductive years. The timing and integration of different events such as union formation, marriage, the establishment of households, and childbearing during these years is of interest. Women from different socioeconomic, racial, ethnic, and cultural backgrounds may time events differently or may establish different patterns of integrating work and family roles (Zambrana, 1987). More research is needed to identify how the sociocultural environment and demographic factors such as race, gender and social class shape attitudes, behaviors, and opportunities which then influence the health and functioning of women of reproductive (Ford Foundation, 1991) or older ages.

The NIMH supports basic, clinical, and applied services research that examines issues relevant to mental disorders or the mental health of older women. The NIMH is particularly concerned with factors and processes that contribute to mental health and adaptation or that may lead to disorder. This interest includes studies of gender differences in psychological processes that may play a role in mental disorder and interpersonal, family, societal, and cultural



processes that may constitute risk or protective factors in relation to mental health outcomes.

Research has demonstrated that health and the aging process are responsive to some degree of intervention and control. By identifying factors in the sociocultural environment that either positively or negatively affect reproduction, adult women's health, and the aging process it is possible to design specific interventions that can improve the health and functioning of women and lead to an overall improvement in the quality of life for women over the lifecourse.

In line with increasing calls for additional research on traditionally ignored women's health issues (Society for the Advancement of Women's Health Research, 1991; Institute of Medicine, 1991; Ory and Warner, 1990; Rodin and Ickovics, 1990), the NIA, the NICHD and the NIMH are targeting the following areas of social and behavioral aspects of women's health and aging for more in-depth examination:

- o Improved healthy life expectancy, psychological adjustment, and quality of life
- o Women's health behaviors, especially in the context of family, work, and community
- o Labor force participation over the lifespan and its relationship to women's well-being, health, and mortality
- o Multiple roles, stress, stress buffers (such as social support), and physical, psychological, and social consequences for women
- o Minorities, special populations and cross-national research

This PA encourages two basic types of research: (1) research on women's special life circumstances and health needs and (2) comparative research of women and men at differing points in the lifecourse, examining antecedents and consequences of gender differences in health status, health behaviors, social role, and life circumstances. The nature of a woman's aging experience and her health across the lifecourse is influenced by a variety of factors, therefore, research is also encouraged on ethnic, socioeconomic, and racial differences; changing gender and economic roles; and the special needs of reproductive aged, middle aged, and older women.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Women's Health Over the Lifecourse: Social and Behavioral Aspects, is related to the priority areas of age-related objectives for adults and older adults and objectives for special populations, including people in minority groups. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-004730-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications for research grants may be made by public and private, for-profit and non-profit organizations, such as universities, colleges, hospitals, and laboratories. Women and minority investigators, in particular, are encouraged to apply. Foreign institutions are not eligible for all mechanisms. Foreign applicants are advised to contact NIA staff to determine eligibility.

#### MECHANISMS OF SUPPORT

Applicants funded under this announcement will be supported through the PHS grant award in accordance with PHS policies applicable to research project grants. All research, career development, and research training mechanisms are applicable.

#### RESEARCH OBJECTIVES

Examples of relevant research topics include, but are not limited to, the following:

##### Improved Healthy Life Expectancy, Psychological Adjustment, and Quality of Life

- o comparisons of healthy life expectancy or mortality rates for men and women, and social and behavioral factors which account for reported differences
- o determination of the impact of co-morbidities (e.g., heart disease, cancer, arthritis, HIV/AIDS) on Activities of Daily Living (ADLs)/Instrumental Activities of Daily Living (IADLs); how various combinations of diseases/illnesses/injuries affect older women's health and functioning
- o identification of precursors (i.e., changing health, social, housing and environment factors, and prior lifecourse experiences) to the high rates of poverty among the oldest-old
- o identification of gender-related factors (i.e., gender-specific tasks and activities) that affect women's coping with physical and/or cognitive problems

##### Women's Health Behaviors

- o understanding why older women have lower rates of preventive health behaviors than younger women for breast cancer and other conditions to which they are particularly vulnerable
- o clarification of the role of socioeconomic and demographic factors, health perceptions, social supports, attitudes about health and aging, and current medical practices in health behaviors and attitudes of women
- o identification of behavioral and social interventions which are effective in motivating women to make greater use of preventive health services across the lifespan
- o identification and examination of social and behavioral components of biological aging, such as menopause



- o examination of underlying psychosocial and physiological processes linking health and behavior in women vs. those operating in men

#### Labor Force Participation

- o studies of the impacts of differences in employment patterns on physical and mental health and quality of life, as well as other outcomes
- o examination of work patterns of women over the life course and their relation to employment opportunities, income levels and related benefits (e.g., health insurance coverage, private pensions, social security)
- o studies of the economic, social and health determinants and consequences for women who do not participate in the labor force, participate intermittently, or who retire early vs. late
- o studies of changing work experience and opportunities in different cohorts of women and the effects on health
- o examination of women's perceptions of job adequacy and perceived control and their relation to physical and mental health
- o examination of changes in labor force participation (e.g., voluntary leaves for child rearing, forced unemployment, part-time employment, retirement) and their relation to changes in health outcomes

#### Multiple Roles of Women, Stress, Stress Buffers and Physical, Psychological and Social Consequences For Women

- o understanding how level of support from spouse or other household members in the presence of multiple roles relates to perceptions of burden and health
- o studies of community and family services that are designed to prevent or alleviate strain associated with caregiving and/or multiple roles (e.g., work/family demands)
- o identification of the impact of employment on health in the presence of multiple family roles and women's perceptions of work in relation to these roles
- o examination of different roles of men and women and how they contribute to gender differences in cognitive functioning, in everyday functioning (e.g., cooking, shopping, and driving), and in the relation between cognitive functioning and everyday functioning
- o examination of how caregiving responsibilities, marital status (divorce, widowhood, single parenthood, cohabitation), and household structure affect health

#### Minorities, Special Populations and Cross-National Research

- o examination of how patterns of family structure, immigration and migration, age and sex ratio, and opportunity for employment affect specific populations of minority women at different points in the lifecourse
- o studies of attitudes toward and the availability, utilization, and quality of health care and other services for women in rural or under-served areas
- o comparative studies of health care, work, family, and economic policies affecting women in different countries
- o studies of differences in abilities of particular women at risk (e.g., low income, immigrant) to adapt to multiple roles and identification of other specific needs

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If minorities and women are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and race/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority populations groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to

include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of minorities or women in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Researchers considering an application in response to this announcement are strongly encouraged to discuss their project, and the range of grant mechanisms available, with NIA, NICHD, or NIMH staff in advance of formal submission. This can be done either through a telephone conversation or through a brief letter of intent giving the descriptive title of the proposed project and identifying the Principal Investigator and, when known, other key participants.

Applicants are to use the research grant application form PHS 398 (rev. 9/91) and PHS 416-1 (rev. 10/91) for Individual Fellowships, available at the applicant's institutional business office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 240, Bethesda, MD 20892, telephone: 301-496-7441. Complete item 2a on the face page of the applications indicating that the applications is in response to this announcement and print (next to the checked box) WOMEN'S HEALTH OVER THE LIFECOURSE: SOCIAL AND BEHAVIORAL ASPECTS.

The PHS 398 application and five legible copies must be mailed to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be assigned to the appropriate group for initial review in accordance with the usual PHS peer review procedures. The review criteria are the traditional considerations underlying scientific merit. Applications will be reviewed for scientific and technical merit by an appropriate initial review group; second-level review will be by the appropriate National Advisory Council. Second-level review of individual fellowship applications will be conducted by the appropriate Institute Executive Group. Applications compete on the basis of scientific merit.

#### AWARD CRITERIA

Applications will compete for available funds with all other applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Marcia G. Ory, Ph.D.  
Behavioral and Social Research Program  
National Institute on Aging  
Gateway Building, Room 2C234  
Bethesda, MD 20892  
Telephone: (301) 496-3136

or

Nancy Moss, Ph.D.  
Demographic and Behavioral Sciences Branch  
National Institute of Child Health and Human Development  
6100 Executive Boulevard, Room 8B13  
Bethesda, MD 20892  
Telephone: (301) 496-1174

or

Mary Ellen Oliveri, Ph.D.  
Personality and Social Processes Research Branch  
Division of Basic Brain and Behavioral Sciences  
National Institute of Mental Health  
Parklawn Building, Room 11C-10  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-3942

Direct inquiries regarding fiscal matters to:

Ms. Linda Whipp  
Grants and Contracts Management Office  
National Institute on Aging  
Gateway Building, Room 2N212  
Bethesda, MD 20892  
Telephone: (301) 496-1472

or

Ms. Melinda B. Nelson  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 505  
6130 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-5481

or

Mr. Bruce L. Ringler  
Chief, Grants Management Branch  
National Institute of Mental Health  
Parklawn Building, Room 7C-15  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-3065

#### Other Interests in This Research Area

Other PHS institutes and agencies are also interested in research dealing with social and behavioral factors affecting women over the lifecourse, including:

The General Clinical Research Centers (GCRC) Program of the National Institutes of Health (NIH) provides inpatient and outpatient research facilities, along with specially trained research nurses, research dietitians and other paraprofessionals to host medical research, including research on behavioral aspects of aging. Additionally, most GCRCs are equipped with computerized data management capabilities, as well as with biostatisticians. Applicants from institutions which have a GCRC funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator must be included with the application.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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Lamphere-Thorpe, Jo-Ann & Robert J. Blendon. Years Gained and Opportunities Lost: Women and Health Care in an Aging America. Project on Women and Population Aging. Southport, Ct.: Southport Institute for Policy Analysis. May, 1991.

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Office of Research on Women's Health. ORWH Research Agenda on Women's Health. Bethesda, MD: National Institutes of Health. March, 1992.

Ory, Marcia G. and Huber R. Warner. Eds. GENDER, HEALTH, AND LONGEVITY: MULTIDISCIPLINARY PERSPECTIVES. New York:

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#### MOLECULAR BASES OF REPAIR AND REGENERATION OF THE AUDITORY RECEPTOR

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA NUMBER: PA-92-106

P.T. 34; K.W. 0715050, 1002004, 1002008

National Institute on Deafness and Other Communication Disorders

#### PURPOSE

The National Institute on Deafness and Other Communication Disorders (NIDCD) invites grant applications addressing the identification of the mechanisms involved in the repair and regeneration of damaged sensory epithelial cells in the auditory periphery. Innovative research on the molecular bases of the repair process should elucidate ways to initiate and control the regeneration of damaged hair cells.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Molecular Bases of Repair and Regeneration of the Auditory Receptor, is related to the priority areas of occupational safety and health; and diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0 or Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

Support mechanisms for this announcement include the individual research project grant (R01) and the First Independent Research Support and Transition (FIRST) Award (R29). Foreign institutions are not eligible for the FIRST Award.

#### RESEARCH OBJECTIVES

##### Background

More than 17 million Americans suffer from sensorineural hearing impairment, which is often attributed to damage to the hair cells of the cochlea. Until recently, damage to these hair cells in mammals was considered to be irreversible. One of the most exciting discoveries of the past decade has been that the auditory sensory epithelia of birds, amphibians, and fish are capable of repair and regeneration after damage by noise or drugs. Studies have shown that the regenerated cells establish functional neural connections. In addition, precursor cells for the regenerated cells have been identified and these precursor cells appear to have mammalian homologues. Recently, regeneration of hair cells from postnatal birds has been achieved in vitro. Further elucidation of these repair and regeneration processes should lead to therapeutic advances.

##### Research Goals and Scope

The ultimate goal of this PA is to gain the knowledge needed to stimulate and control the repair processes involved in hair cell regeneration so that sensorineural hearing loss due to hair cell damage might be prevented or reversed. Investigation of the molecular and cellular mechanisms involved in the initiation and control of this repair process is amenable to methods of modern biotechnology. Innovative, multidisciplinary, state-of-the-art studies are encouraged to determine the factors that initiate and control sensory cell replacement and recovery of hearing.

Studies may include, but are not limited to, the topics listed below:

- o improved models of hair cell damage such that the resulting auditory impairment is less variable, and therefore easier to control and study;
- o more specific identification of the cellular precursors of the replacement hair cells and supporting cells;
- o identification of the factors that trigger the regeneration response in the hair cell epithelia;
- o definition of the role of known mitotic growth factors and other chemical agents (for example, retinoic acid) that may control and/or trigger progenitor cell division;



- o development of pharmacologic agents for inducing and controlling cell replacement and auditory recovery;
- o investigation of the molecular and cellular bases for hair cell regeneration in the mammalian ear;
- o assessment of the contribution of other potential repair processes in the ear, including repair of damaged subcellular components of hair cells and repair of damaged links between sensory cells and the overlying tectorial membrane;
- o evaluation of the role and extent of the re-establishment of neuronal connections in the sensory organ for their contribution to the recovery of hearing; and
- o correlation of structural changes with measures of functional changes during the course of regeneration.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS.

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants/offerors are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions.

Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

The completed original application and five exact copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate national advisory council.

## AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered as funding decisions are made:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

## INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Amy Donahue, Ph.D.  
Chief, Hearing Program  
Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Suite 400-B  
Rockville, MD 20892  
Telephone: (301) 402-3458  
FAX: (301) 402-6251

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Grants Management Officer  
Division of Extramural Activities  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Suite 400-B  
Rockville, MD 20892  
Telephone: (301) 402-0909

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## HEARING IMPAIRMENT AND OTHER COMMUNICATION DISORDERS ASSOCIATED WITH CMV INFECTION, HIV INFECTION, AND AIDS

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA NUMBER: PA-92-107

P.T. 34; K.W. 0715050, 0715008

National Institute on Deafness and Other Communication Disorders

## PURPOSE

The Division of Communication Sciences and Disorders of the National Institute on Deafness and Other Communication Disorders (NIDCD) encourages grant applications seeking support for innovative research in the area of hearing impairment and other communication disorders in persons with cytomegalovirus (CMV) infection, human immunodeficiency virus (HIV) infection or with acquired immunodeficiency syndrome (AIDS). Research is needed to clarify the role of CMV, HIV, AIDS, and therapeutic agents used in the treatment of these diseases in the etiology of hearing loss and other communication disorders.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Hearing Impairment and Other Communication Disorders Associated with CMV Infection, HIV Infection, and AIDS, is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0 or Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

Support mechanisms for the announcement include the individual research project grant (R01) and the First Independent Research Support and Transition (FIRST) Award (R29). Foreign institutions are not eligible for the FIRST Award.

## RESEARCH OBJECTIVES

### Background

Congenital CMV infection is the leading cause of nonhereditary deafness in children. The most frequent sequela associated with congenital CMV infection is hearing loss. It has been estimated that congenital CMV infection accounts for about 40,000 cases of sensorineural hearing loss per year in the United States.

Some studies have shown that more than 90 percent of AIDS patients are co-infected with CMV. Current estimates from the Centers for Disease Control indicate that over 1.7 million Americans are infected with HIV. During the course of the disease, the infection progresses in stages from an initial asymptomatic state, to AIDS-related complex, and AIDS characterized by systemic immune deficiency and opportunistic infection. Case reports indicate that auditory and vestibular dysfunction may occur in HIV-infected persons and the symptoms may develop in early stages of infection. Although infection of the central nervous system by HIV is well documented, the pathophysiology of auditory impairment in HIV-infected individuals is not known. Hearing disorders in AIDS patients could be caused by infection of the cochlea and auditory nerve with CMV or HIV. Additionally, hearing loss in these patients could be due to other opportunistic infections or treatment with ototoxic antimicrobial therapeutic agents. Studies are needed to document auditory abnormalities in CMV- and HIV-infected persons so that appropriate early treatment might be provided.

In addition to auditory and vestibular disorders, patients with AIDS may experience other communication difficulties. Kaposi sarcomas often occur in the mouth, pharynx, and larynx and can cause respiratory, swallowing, phonatory and articulatory difficulties. Neurogenic components associated with AIDS may include both motor speech and language disorders. An estimated 20,000 to 30,000 children in the United States are HIV positive; thus, speech-language pathologists, audiologists, and otolaryngologists are inevitably involved in the diagnosis and treatment of CMV- and HIV-positive children.

### Research Goals and Scope

Improved treatment for AIDS patients has increased the postdiagnosis quality and expectation of life. Disorders of hearing, balance, smell, taste, speech, voice, and language represent a quality of life issue that increases in importance as the survival period is extended in HIV-infected individuals.

The ultimate goal of this announcement is to increase the understanding of the etiology and pathophysiology of communication impairments during CMV infection, HIV infection, and AIDS and to use this information to improve treatment and quality of life. Innovative, state-of-the-art, multidisciplinary clinical and basic studies are encouraged.

Studies may include, but are not limited to, the topics listed below as they relate to the communication disorders of hearing, balance, taste, smell, voice, speech, and language:

- o development of quantitative, objective techniques for early detection, evaluation, and prognosis of developing communication dysfunction in CMV- and HIV-infected persons;
- o establishment of an epidemiological surveillance system to estimate the incidence and prevalence of communication disorders due to these viral infections in different populations;
- o development of the means for identifying and classifying communication disorders in CMV- and HIV-infected children and adults;
- o examination of the potential ototoxic properties of antifungal, antibacterial, and antiviral agents (such as zidovudine, zalcitabine, and didanosine);
- o determination of the pathophysiology of these viral infections within the peripheral and central auditory nervous system;
- o identification of the cellular and molecular mechanisms specific to these viral infections of sensory cells;
- o identification of the specific intra- and extracellular biochemical, metabolic, enzymatic, and protein changes associated with these viral infections of sensory cells;
- o development of animal or in vitro models to address the viral pathogenesis in sensory cells and tissues in immunocompetent and immunodeficient subjects;
- o examination and correlation of the interactions between primary infection and opportunistic cofactors in exacerbating damage to sensory cells and tissues (including cytomegalovirus, pneumocystis carinii, and candidiasis);
- o examination of maternal immunosuppression effects on the pathogenesis of CMV infection in the placenta and fetal auditory system;
- o assessment of CMV infection, HIV infection, or AIDS on communication disorders throughout the life cycle, including critical developmental periods and aging; and
- o determination of appropriate communicative and sensory therapeutic and rehabilitative protocols for communication disorders associated with CMV infection, HIV infection, and AIDS.

### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk



of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether or not the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research differ from the standard deadlines and are found in the PHS 398 instructions.

Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441. The title and number of this announcement must be typed in Section 2a on the face page of the application.

The completed original application and five exact copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate National Advisory Council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered as funding decisions are made:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

For additional information regarding programmatic issues, investigators are encouraged to call or write to NIDCD staff responsible for grants in the investigator's particular area of scientific interest:

Dr. Beth Ansel (voice, speech)	(301-402-3461)
Dr. Judith Cooper (language)	(301-496-5061)
Dr. Amy Donahue (hearing)	(301-402-3458)
Dr. Jack Pearl (taste)	(301-402-3464)
Dr. Rochelle Small (smell)	(301-496-3464)
Dr. Daniel Sklare (balance/vestibular)	(301-402-3461)



Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Suite 400-B  
6120 Executive Boulevard  
Rockville, MD 20892

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Grants Management Officer  
Division of Extramural Activities  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Suite 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-0909

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### TRAVEL FELLOWSHIPS FOR UNDERREPRESENTED MINORITY STUDENTS IN COMMUNICATION SCIENCES AND DISORDERS

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA NUMBER: PA-92-108

P.T. 42, 48; K.W. 0715050, 0715055

National Institute on Deafness and Other Communication Disorders

#### PURPOSE

The National Institute on Deafness and Other Communication Disorders (NIDCD) encourages participation of minority students in scientific meetings and research forums related to communication sciences and disorders. The purpose of this Program Announcement (PA) is to encourage those organizations planning to submit conference grant applications (R13) to NIDCD to include requests for support of travel by minority students to those meetings. In addition, conference grant applications limited to support for minority student travel are encouraged from the sponsoring organizers of scientific meetings and conferences.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Travel Fellowships for Minority Students in Communication Sciences and Disorders, is related to the priority area of special population objectives. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0 or Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

The support mechanism for grants in this area will be the conference grant (R13).

#### RESEARCH OBJECTIVES

The small number of African-American, Hispanic-American, Native American, and Pacific Islander individuals electing research careers is conspicuous in all areas of science. The number of minority researchers in this country is much lower than would be expected from the proportion of the population comprising minorities. Most particularly, there is notable underrepresentation of ethnic minority scientists in the communication sciences. Preparation for research in the communication sciences and disorders involves training in one or more of a variety of disciplines, including otolaryngology, speech-language pathology, audiology, auditory and chemosensory psychophysics, and the anatomy, biochemistry, pharmacology and physiology, and molecular biology and genetics related to hearing, balance, smell, taste, voice, speech and language. In each of these disciplines, recruitment and retention of minority students for research careers has lagged.

By supporting minority student attendance at scientific meetings, the NIDCD anticipates that exposure to basic and clinical research developments will encourage their participation in communication sciences and disorders. Information on research opportunities will be made available to those students. Attracting undergraduate, graduate, and postdoctoral students from minority groups to the communication sciences and disorders should increase the number of active researchers in these areas. The NIDCD encourages conference grant applications (R13) which include a component related to travel support for minority students, as well as overall support for the conference. In addition, conference grant applications limited to support of minority student travel are encouraged from the sponsoring organizers of scientific

meetings and conferences. A mentor specifically-assigned to each student is required.

Issues to be addressed include, but are not limited to, the following:

- o A plan for the recruitment and selection of students, including selection committee and criteria for selection
- o Number and level of students to be selected
- o Minority group(s) to be targeted
- o Advertisement of availability of travel fellowships
- o The conference: purpose, content and scope; research elements or foci; justification of value of conference to minority student
- o The mentor: selection; qualifications, for example, research expertise, previous grant support, prior mentoring experiences; role of mentor prior to, during, and after the conference; plans for monitoring mentor
- o Activities during conference, such as opportunities for contact with other researchers in attendance, special workshops and discussions, and announcement of the student recipients
- o Evaluation of the conference experience by students
- o Justification of associated costs

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. In addition, applicants are encouraged to obtain specific guidelines for the preparation of a conference grant application.

Application kits and conference grant guidelines are available from most institutional offices of sponsored research, the NIDCD Program Administrator cited below, and the Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit following the customary PHS peer review procedures.

#### AWARD CRITERIA

Applications will compete for available funds with all other applications received. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds

#### INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Judith A. Cooper, Ph.D.  
Deputy Director, Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 496-5061  
FAX: (301) 402-6251

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Grants Management Officer  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-0909

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA NUMBER: PA-92-109

P.T. 34; K.W. 0404009, 1002008, 0710070, 0745027, 0760075

National Institute on Drug Abuse

#### PURPOSE

The National Institute on Drug Abuse (NIDA) invites research grant applications for studies on the discovery/development of antibodies, enzymes, or catalytic antibody substances as potential treatments to reduce cocaine use. The proposed medication would provide either active or passive protection against the pharmacodynamic/neurotoxicological action of cocaine. It is anticipated that the proposed medication could function by rapidly reducing the concentration of the cocaine in plasma or serving as a novel antagonist. Within this general field of research, special emphasis should be placed on (1) using a novel protein to block receptor sites through competitive inhibition, (2) using catalytic antibodies to rapidly react with the abused substance and convert the substance into a nonactive species, (3) using anti-idiotypic based vaccines to produce antibodies that bind with cocaine and reduce its free plasma concentration, (4) using monoclonal antibodies to bind with the abused substance and reduce its effective concentration in the plasma, and/or (5) enhancing the body's own natural ability to eliminate cocaine.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Development of Immunological and Molecular Biological Approaches to Effect Reduction of Cocaine Use, is related to the priority of health promotion (alcohol and other drugs). Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20492-9325, telephone 202-738-3238.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, non-profit and for-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, research institutions, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign applicants are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29).

#### MECHANISM OF SUPPORT

Support mechanisms include Research Projects (R01), the small grant (R03), and the FIRST Award (R29). Most investigator-initiated research is supported by research grants. Research grants are awarded to institutions on behalf of Principal Investigators who have designed and will direct a specific project or set of projects. For information on the special requirements of the FIRST awards (R29), and small grants (R03), please contact the program staff listed under INQUIRIES.

#### RESEARCH OBJECTIVES

##### Background

Drug abuse, including the use of cocaine, is an addictive disorder that continues to be a burden on societies throughout the world. It is directly associated with crime and the spread of infectious diseases, notably venereal disease and especially AIDS. The existing psycho-pharmacological medications used to treat disorders such as depression and mania have not been wholly successful in treating drug abuse disorders. It is generally believed that there is much room for advancement in the treatment of addictive disorders. A large portion of the addicted population have not been reached and are not enrolled in drug treatment programs. Further, the retention of patients in these programs, particularly for cocaine use is very low. Most cocaine addicts do not actively seek help. The development of an effective treatment for cocaine use is a top priority of the NIDA.

The conventional method to discover and develop pharmacotherapeutic agents for substance abuse is to find a receptor site for the abused substance and to screen many compounds for activity at the receptor. For opiates, this approach has been successfully demonstrated; currently, there are two drugs, methadone and naltrexone, approved by the FDA for the treatment of opiate addiction. Methadone, an agonist, serves as a maintenance drug while naltrexone, an antagonist, serves to block opiate effects. Medications presently under clinical evaluation for the treatment of opiate addiction include buprenorphine, a partial agonist; acetylmethadol, a long-acting agonist; and nalbuphine, an antagonist. Research is actively being encouraged for the development of other agonist, antagonist, and opiate peptides as potential candidates for the treatment of narcotic addiction.

In contrast to the success that has been achieved in the treatment of opiate abuse, no medication has yet been approved for the treatment of cocaine addiction. Clinical studies are currently underway for the evaluation of the efficacy of a number of drugs, such as buprenorphine, carbamazepine, desipramine, mazindol, flupenthixol, nifedipine, and amantadine for the treatment of cocaine addiction. These studies have been open label or conducted in less than 200 subjects. It may be concluded from these clinical trials that research to develop a treatment agent for cocaine addiction must continue.

Recent advances in the field of molecular biology, particularly in the area of catalytic antibodies and the development of anti-idiotypic based vaccines, suggest that now is the time to apply this technology to developing new, biologically-based medications for cocaine use. Cocaine is a diester and is hydrolyzed to less active metabolites; the metabolites are water soluble and are excreted from the body. The thrust of the approach would be to develop biological systems that either rapidly bind with plasma cocaine (as antibodies) or that rapidly hydrolyze cocaine to a water soluble



metabolite (as a catalytic antibody). The result would be to effect a lower (unbound) plasma level of cocaine and/or a shorter duration of cocaine in the body. In addition, it would be appropriate to consider a means of extending the duration of the therapy for reasons of patient compliance and for reasons of relapse prevention. Development of an "anticocaine vaccine," that would be triggered only when the abused drug was taken, would be ideal. Developing a means of stimulating the intrinsic capacity to hydrolyze cocaine is considered an interesting approach which is consistent with diminishing the adverse pharmacological and toxicological effects of a given dose of cocaine.

In the applications, programmatic emphasis should be placed on innovation in design and development. To qualify for this program, applications should embody unique and/or innovative theoretical constructs with an experimental approach leading to a new system of drug abuse therapy. The application must detail how these constructs and approaches are consistent with developing a treatment for cocaine use.

#### Areas of Interest

The areas of research interest that may be funded include those that are innovative, that develop new methods of drug discovery for cocaine use pharmacotherapies, and that will advance the development of a new medication for the treatment of cocaine use. In general, these may include:

- o Using antibodies to bind with the abused substance.
- o Using antibodies or enzymes to increase the natural rate of metabolism of the abused drug.
- o Developing techniques for blocking the receptor site through competitive inhibition. The approach should be based on molecular biology in order to be compatible with this program.
- o Developing procedures that enhance the intrinsic capacity to eliminate the abused substance.

These areas of research interest are not intended to be all-inclusive and alternate or similar areas will be considered. However, experimental models to develop therapeutic interventions for cocaine use are extremely limited at the present time. Therefore, a major research effort is required to design innovative approaches to expand the current methods and models to those that have not been explored.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application receipt dates indicated in the application kit.



Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquires, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in item 2a on the face page of the application.

FIRST Award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

The Division of Research Grants serves as a central point of receipt of applications for most discretionary PHS grant programs. Applications received under this announcement will be assigned to an Initial Review Group (IRG) in accordance with established PHS Referral Guidelines. The IRG, consisting primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit. Notification of the review recommendations will be sent to the applicant after this initial review. Applications will receive a second-level review by an appropriate National Advisory Council whose review may be based on policy considerations as well as scientific merit. Only applications recommended for further consideration by the Council may be considered for funding.

#### Review Criteria

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by an initial review group in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate National Advisory Council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Availability of funds
- o Quality of the proposed project as determined by peer review
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is encouraged.

Direct inquiries regarding programmatic issues to:

James B. Terrill, Ph.D.  
Medications Development Division  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 11A-55  
Rockville, MD 20857  
Telephone: (301) 443-6270

Direct inquiries regarding fiscal matters to:

Mrs. Shirley A. Denney  
Chief, Grants Management Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-55  
Rockville, MD 20857  
Telephone: (301) 443-6710

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.279. Awards are made under authorization of the Public Health Service Act, sections 301 and 515 (42 USC 241 and 290cc) and administered under PHS grants policies and Federal Regulations 42 CFR 92 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### DEVELOPMENT OF THEORETICALLY-BASED PSYCHOSOCIAL THERAPIES FOR DRUG DEPENDENCE

NIH GUIDE, Volume 21, Number 34, Part II, September 25, 1992

PA NUMBER: PA-92-110

P.T. 34; K.W. 0404009, 0745060, 0404000

National Institute on Drug Abuse

NIH Guide for Grants and Contracts - Vol. 21, No. 34, Part II of II - September 24, 1992

## PURPOSE

The purpose of this announcement is to encourage the development, refinement, and pilot efficacy testing of theoretically based psychosocial interventions for drug dependence, including psychotherapies, behavioral and cognitive-behavioral therapies, and counseling strategies. In this Program Announcement (PA), "therapy development" includes both the development of new therapies and the modification of existing therapies. The development of drug dependence treatment therapies based upon therapy-specific diagnostic approaches is particularly encouraged. The ultimate goal of this PA is to increase the efficacy of drug dependence treatment by developing therapies that are finely tailored to the specific needs and problems of the drug-dependent individual. This announcement is not intended to support full-scale clinical trials.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Development of Theoretically Based Psychosocial Therapies for Drug Dependence, is related to the priority areas of alcohol and other drugs. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

Support mechanisms include: Research Projects (R01), Small Grants (R03), and First Independent Research Support and Transition (FIRST) Awards (R29). Most investigator-initiated research is supported by research grants. Research grants are awarded to institutions on behalf of Principal Investigators who have designed and will direct a specific project or set of projects. Most grants can be renewed at intervals or supplemented through the formal submission and review process described below. Except for Small Grants (R03) and FIRST Awards (R29), investigator(s) may apply for a renewal (competing continuation) of the project by submitting an application for further support, including a report of progress and including specific plans for future work. For details on a particular support mechanism or program, please contact the program staff listed at the end of this announcement. Foreign institutions are not eligible for the FIRST Award (R29s).

## RESEARCH OBJECTIVES

### Background

Although several psychosocial treatments for drug-dependent individuals currently exist, many were initially developed for individuals with problems other than drug dependence. While the drug abuse treatment research community has adapted many of these therapies to meet the needs of the drug-dependent individual, more can be done in the development of new, and the modification of existing, therapies for drug dependence.

Theory-driven therapies specifically created/modified for drug abuse/dependence treatment need to be operationalized, manualized, measured, and pilot tested before efficacy testing through rigorously controlled clinical trials can occur. As is the case with medications development, the development of psychotherapeutic and behavioral interventions is a time consuming and costly procedure. Until this point, there has been, paradoxically, support available for the efficacy testing of drug abuse therapies, but no support for their initial development, refinement, and pilot testing. Based in part upon recommendations made to the National Institute on Drug Abuse by experts in the drug abuse treatment field, this program announcement intends to provide support for this endeavor.

### Specific Areas of Interest

Investigators are encouraged to submit applications to develop new or modify existing psychosocial therapies that: (1) appear promising for the treatment of drug-dependent individuals and (2) have a convincing rationale. Therapies of interest include, but are not limited to, the following:

- o Diagnosis-specific or client characteristic-specific theoretically based therapies for drug dependence. Such therapies are based upon theories regarding measurable psychological, behavioral, or interpersonal constructs. Examples include therapies to overcome cognitive deficits, family dysfunction, or social skill deficiencies, where "diagnoses" may be given regarding the relevant cognitive abilities, family functioning, or social skills. As appropriate, investigators are encouraged to propose the development of relevant diagnostic instrument(s) in addition to the development of the therapy, in their applications.

It should be noted that in the context of this PA, "diagnosis" is not limited to traditional DSM-III-R or DSM-IV classification. Rather, it may refer to any measurable, theoretically based psychological, behavioral, or interpersonal construct.

- o Theoretically-based therapies to treat dependence upon certain types of drugs (e.g., cocaine, heroin, marijuana, benzodiazepines).
- o Theoretically-based therapies to treat particular clients with one or more co-morbid mental disorders (e.g., mood, anxiety, or personality disorders).
- o Theoretically-based therapies to treat clients of a particular ethnic, racial, or cultural group where it is hypothesized that a therapy geared specifically toward that group will be more effective than currently existing therapies.
- o Theoretically-based therapies oriented to the special needs of women.
- o Any drug dependence therapy or counseling strategy, including therapies which are "eclectic" or pragmatically based,

that have a convincing rationale.

A goal of this PA is to encourage projects involving the development of new or refinement of existing therapies and counseling strategies which are based upon a theoretical rationale. Therapy development applications should include an explicit statement describing the theoretical and clinical basis for that therapy, and the population for whom it is intended. Applicants proposing the development of "eclectic" or "pragmatic" therapies, which may not be tied to a single theoretical orientation, should describe the rational, practical and clinical basis for the therapy. Diagnosis-specific or client characteristic-specific therapies are particularly encouraged for development. A thorough literature review documenting and explaining relevant research and clinical findings which support and apparently contradict the stated rationale should be included. Relevant clinical observations and anecdotal reports are particularly encouraged where relevant research findings are lacking. The nature of the therapy to be developed should be described in as much detail as possible. Components of the therapy or counseling approach to be developed should be operationally defined wherever possible.

Applicants proposing diagnosis-specific or client-characteristic-specific therapies must address the issue of whether there is a need for development of theoretically based diagnostic systems or client assessment scales tailored to their therapy. If one theorizes, for example, that certain heroin addicts either began or maintained heroin use due to interpersonal conflicts, and that the resolution of these conflicts will decrease drug use, a measure of interpersonal conflicts should either exist, or be developed with a therapy based upon treating these conflicts. The development of a theoretically based therapy should include measures of client attributes directly related to that therapy. As part of the research activity supported under this announcement, investigators are encouraged to develop new or refine existing diagnostic systems/client assessment scales necessary to measure the impact of the proposed theoretically based therapy. Methods that will be used to develop these instruments should be described in detail. Close attention should be paid to the psychometric characteristics of these measures (i.e., their validity, internal consistency, inter-rater and test-retest reliability).

Applicants must also address the issue of how they intend to measure what is actually occurring in the therapy they are proposing to develop. The credibility of any treatment research depends on our ability to determine the extent to which that treatment was actually administered, and administered correctly. In the development of any therapy, therefore, emphasis should be placed upon the development of psychometrically sound therapist competence and adherence scales, process measures, and instruments measuring the integrity and fidelity of the therapy. Applicants must describe the instruments they intend to develop, and the methods that they will use to ensure they are developing valid and reliable measures.

In the development of a new therapy for drug dependence, a broad range of issues relevant to efficacy and safety should be addressed. Pilot efficacy testing of newly developed/modified therapies, therefore, should be considered an integral part of any therapy development process. The applicant must describe, in detail, the nature of any pilot testing proposed. While a full-scale, controlled clinical trial of a therapy is not expected as part of this PA, any pilot testing proposed must be based upon sound, scientific methods.

When pilot testing, if a subject is identified as being at risk for HIV acquisition and/or transmission, HIV testing and counseling should be offered to the subject in accordance with current guidelines. Furthermore, in high-risk populations, investigators are encouraged to assess the effect of the new therapy on the acquisition/transmission of associated infectious disease, including HIV.

#### STUDY POPULATIONS

##### NATIONAL INSTITUTES OF HEALTH (NIH) POLICY CONCERNING INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

Applications for grants and cooperative agreements and proposals for contracts that involve human subjects are required to include minorities and both genders in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders, and conditions which disproportionately affect them. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages. If one gender and/or minorities are excluded or are inadequately represented in this research, particularly in proposed population-based studies, a clear compelling rationale for exclusion or inadequate representation should be provided. The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., American Indians or Alaskan Natives, Asians or Pacific Islanders, Blacks, Hispanics). Investigators must provide the rationale for studies on single minority population groups.

Applications for support of research involving human subjects must employ a study design with minority and/or gender representation (by age distribution, risk factors, incidence/prevalence, etc.,) appropriate to the scientific objectives of the research. It is not an automatic requirement for the study design to provide statistical power to answer the questions posed for men and women and racial/ethnic groups separately; however, whenever there are scientific reasons to anticipate differences between men and women, and racial/ethnic groups, with regard to the hypothesis under investigation, applicants should include an evaluation of these gender and minority group differences in the proposed study. If adequate inclusion of one gender and/or minorities is impossible or inappropriate with respect to the purpose of the research, because of the health of the subjects, or other reasons, or if in the only study population available there is a disproportionate representation of one gender or minority/majority group, the rationale for the study population must be well-explained and justified.

The NIH funding components will not make awards of grants, cooperative agreements or contracts that do not comply with this policy. For research awards which are covered by this policy, awardees will report annually on enrollment of women and men, and on the race and ethnicity of subjects.



## APPLICATION PROCEDURES

Applications are to be submitted on the research grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The special receipt dates for applications for AIDS-related research are found in the PHS 398 instructions. Application kits are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of the announcement must be typed in Item 2a on the face page of the application.

FIRST Award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original application and five legible copies of the complete application must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

## REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by an initial review group in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate National Advisory Council. Small grant (R03) applications assigned to the NIDA do not receive a second-level review.

## AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Institute program needs and balance

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Lisa Onken  
Treatment Research Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 10A-30  
Rockville, MD 20857  
Telephone: (301) 443-4060

Direct inquiries regarding fiscal matters to:

Mrs. Shirley Denney  
Chief, Grants Management Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.279. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act (42 USC 241 and 284) and administered under PHS grants policies and Federal Regulations at Title 42 CFR Part 52, "Grants for Research Projects," Title 45 CFR Part 74 & 92, "Administration of Grants," and 45 CFR Part 46, "Protection of Human Subjects." Title 42 CFR Part 2 "Confidentiality of Alcohol and Drug Abuse Patient Records" may also be applicable to these awards. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## MINORITY HIGH SCHOOL STUDENT RESEARCH APPRENTICE PROGRAM

NIH GUIDE, Volume 21, Number 34, September 25, 1992

PA NUMBER: PA-92-111

P.T. 34, FF; K.W. 0710030, 0720005

National Center for Research Resources

Application Receipt Date: December 1, 1992



## PURPOSE

The National Center for Research Resources (NCRR), National Institutes of Health (NIH), currently plans to continue and expand the Minority High School Student Research Apprentice Program (MHSSRAP) in 1993. The purpose of the program is to provide minority high school students with a meaningful experience in various aspects of health-related research in order to stimulate their interest in careers in science.

In FY 1993, the program is expanding the science teacher initiative to include not only in-service elementary, middle, junior, and senior high school teachers, but also potential K-12 science teachers in pre-service education programs. Eligible teachers will still be those who are members of a minority group or who teach a significant number of minority students. Teachers may participate in the program for a second year. The hands-on summer research project must be structured to update the teachers' knowledge and skills in modern research tools and techniques as well as to strengthen their teaching skills. The experience should provide teachers the opportunity to bring back to the classroom a sense of the excitement of research that would stimulate students to pursue scientific careers. A longer range goal is to establish year round linkages between pre-service and in-service science teachers, elementary and secondary school students, and biomedical researchers.

Please note, however, that expansion of the program in FY 1993 is contingent on the availability of appropriated funds. Thus, allocations may be reduced below the amount requested in the application. Upon recommendation of the National Advisory Research Resources Council, the NCRR will give preference in making awards to those institutions that can support a summer program having a "critical mass" of at least five or six students.

## ELIGIBILITY REQUIREMENTS

Eligible institutions are those that were eligible for a Biomedical Research Support Grant award in FY 1992 or are awardees of the Minority Biomedical Research Support (MBRS) Program. ALL ELIGIBLE INSTITUTIONS, INCLUDING THOSE NOT CURRENTLY OR PREVIOUSLY FUNDED UNDER THE MHSSRAP, ARE STRONGLY ENCOURAGED TO APPLY. Only one application for the Apprentice Program may be submitted by a component of an institution that is BRSG-eligible in FY 1992 and the recipient of an MBRS award.

Under-represented minority students and teachers are defined as individuals who identify themselves as Black, Hispanic, Native American, Pacific Islander, or any particular ethnic or racial group which has been determined by the grantee institution to be under-represented in biomedical or behavioral research.

Participants eligible for support must be U.S. citizens or have a permanent visa. Eligible students are those who are enrolled in high school during the 1992-1993 academic year. (Students who will graduate from high school in 1993 are eligible, as is a student who participated in a previous year provided he/she is still enrolled at the high school level.)

## MECHANISM OF SUPPORT

The mechanism of support for this program will be the NIH grant-in-aid (S03).

Awards will be for one year beginning March 1, 1993, contingent upon availability of appropriated funds. Support will be provided at a level of \$2,000 for each student apprentice, \$3,000 for each pre-service teacher, and \$5,000 for each in-service science teacher. Applications may request both students and teachers or students only. No indirect costs will be paid. Direct support must be as salary; stipends are not allowed. Funds allocated may also be utilized for supplies, extending the research experience, or if adequate funds exist, for the addition of a student apprentice. However, funds from these grants may only be used for the costs of the apprentice program. The Program Director is responsible for the recruitment and selection of the apprentices and science teachers and assignment of each to an appropriate investigator.

Students. Recruitment and selection of students must emphasize factors including the student's motivation, ability, scholastic aptitude, and accomplishments. In addition, consideration must be given to science teachers' recommendations and, whenever possible, the degree of parental commitment. Assignments must be made to investigators involved in health-related research who are committed to increasing the high school student's understanding of research and the technical skills needed.

Teachers. Recruitment and selection criteria for in-service teachers must include: experience and teaching responsibilities, level of interest in participating in a research program, expected impact on their teaching programs, ability to stimulate minority students to pursue scientific careers, and future plans for continued interaction with the research institution. Potential teachers should be enrolled in pre-service programs and have an expressed interest in teaching life sciences at the K-12 level.

## APPLICATION PROCEDURES

The application consists of (a) a letter stating the justification for the number of student and teacher positions requested (preference will be given to those institutions with a demonstrated commitment and a documented history of encouraging students to pursue scientific careers) and (b) the original and one signed and completed copy of the face page, page 4 "Detailed Budget for First 12-Month Budget Period Direct Costs Only," and checklist page of the grant application form PHS 398 (rev. 9/91). The required pages of the PHS 398 application form must be completed according to instructions provided in the PHS 398 (rev. 9/91) kit except for the following:

Face Page

Item 1 - Leave blank.

Items 2a and 2b - Check the box marked "YES" and type in the number and title of this Program Announcement.

Items 4 and 5 - Not applicable; do not complete.

Item 6, Dates of entire proposed project period - Enter 03-01-93 through 02-28-94.

Item 7 and 8 - Insert the total dollar amount of the request, which is the sum, from application page 4, of the number of student positions requested times \$2,000 per student; the number of pre-service teachers requested times \$3,000; and the number of in-service teachers times \$5,000. No indirect costs will be provided; thus the direct and total costs will be the same.

Item 14, Organizational component to receive credit towards a Biomedical Research Support Grant - Use this space to enter the code on which eligibility for this MHSSRAP application is based (no credit will be given for the S03 application). Also use this space to enter the BRSG and/or MBRG grant number(s) if available.

Page 4, "Detailed Budget for First 12-Month Budget Period Direct Costs Only" - Using ONLY the Other Expenses category, enter on separate lines the number of students requested at \$2,000 per student; the number of pre-service teachers requested at \$3,000 per teacher; and the number of in-service science teachers requested at \$5,000 per teacher.

Enter the sum of the amounts requested for each under the "TOTALS" column for the Other Expenses category and under "Total Direct Costs for First 12-Month Budget Period" at the bottom of the page.

The original and one copy of the student and teacher report(s), signed by the Program Director, must be submitted with the renewal application by December 1 so that the data contained in these reports can be used by NCRR to decide about policies and future funding for the MHSSRAP.

These reports must also be submitted at the same time even if renewal support is not requested. All reports, including the Financial Status Report, must be submitted to the NIH by the grantee institution no later than May 31, 1993, unless an extension of the budget period end date has been authorized in writing.

Applications must be received by December 1, 1992 by:

Office of Grants and Contracts Management  
National Center for Research Resources  
National Institutes of Health  
Westwood Building, Room 849  
5333 Westbard Avenue  
Bethesda, MD 20892

(Do NOT mail the application to the Division of Research Grants, NIH.)

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Marjorie A. Tingle, Ph.D.  
Director, Biomedical Research Support Program  
National Center for Research Resources  
Westwood Building, Room 10A-11  
5333 Westbard Avenue  
Bethesda, MD 20982  
Telephone: (301) 496-6743.

Direct inquiries regarding fiscal matters to:

Ms. Mary V. Niemiec  
Supervisory Grants Management Specialist  
Office of Grants and Contracts Management  
National Center for Research Resources  
Westwood Building, Room 849  
5333 Westbard Avenue  
Bethesda, MD 20982  
Telephone: (301) 496-9840.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.337, Biomedical Research Support. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (a)(3); Public Law 78-410 (42 USC 241) as amended, and administered under PHS grants policies and Federal Regulations 45 CFR 74 and the Guidelines for Minority High School Student Research Apprentice Program. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

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# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

Vol. 21., No. 35  
October 2, 1992

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES

AVAILABILITY OF RESOURCE FOR DIETARY INTAKE AND NUTRITION RESEARCH

NIH GUIDE, Volume 21, Number 35, October 2, 1992

P.T. 34; K.W. 0710095, 0780000

National Heart, Lung, and Blood Institute

The Nutrition Coordinating Center (NCC) at the University of Minnesota is a unique national resource available for dietary data collection and nutrient calculation for epidemiological studies, clinical trials, and other medical research studies. The center provides standardized procedures for collecting food intake data and calculating nutrient intakes at the high level of specificity needed for investigations of the relationship between diet and disease.

Investigators can use the services of the NCC in two ways. They can license use of the Minnesota Nutrition Data System (NDS). NDS is microcomputer-based software for interactive dietary data collection and nutrient calculation. NDS prompts the user to describe food intake at the level of detail required for dietary research and calculates the nutrient content of the intake. Then NDS presents the data on the screen, in printed reports, or in ASCII files that can be merged with other study data using statistical analysis software. The



NDS database allows the user to describe over 150,000 foods and 6,000 brand name products. The database contains values for up to 93 nutrients, including soluble and insoluble fiber fractions, 23 individual fatty acids, and 18 amino acids. NDS can be used to guide 24-hour dietary recall interviews or to process food intake records. NDS can also be used to collect and analyze diet histories and to calculate the nutrient content of recipes or menus. A customized version of NDS is being used in the National Health and Nutrition Examination Survey (NHANES III) to collect dietary data from more than 30,000 Americans.

Alternatively, investigators can send dietary intake records to NCC for processing. Data collection and processing procedures can be customized to meet the needs of specific studies. Investigators may reanalyze data collected in the past to take advantage of improved analytical data and new nutrients added to the database. Over the past 18 years, NCC has processed more than 300,000 records.

NCC also provides a two-day training program for dietary interviewers. For investigators who send dietary intake records to NCC for processing, the training ensures the use of standardized data collection procedures tailored to the research protocol. Interviewers are certified following satisfactory completion of the training program and follow-up exercises. For investigators using the NDS directly, the training is designed to enhance use of the software to meet research protocol requirements. Over the past 18 years, NCC has trained and certified more than 700 dietary interviewers.

NCC receives major support from the National Heart, Lung, and Blood Institute, the National Cancer Institute, and the National Center for Health Statistics. NCC services and software are used by investigators in academia, government, non-profit organizations, and industry. Users are required to pay a fee to cover part of the operational costs.

For information and fee schedules, contact Marilyn Buzzard, Ph.D., Director, Nutrition Coordinating Center, 2221 University Avenue, SE, Suite 310, Minneapolis, MN 55414, telephone (612) 627-4869, FAX (612) 627-4191.

#### INQUIRIES

Abby Ershow, Sc.D.  
Lipid Metabolism - Atherogenesis Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Bethesda, MD 20892  
Telephone: (301) 496-1681  
FAX: (301) 496-9882

#### HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 35, October 2, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

#### SOUTHWESTERN WORKSHOP

DATES: November 16 & 17, 1992

LOCATION:  
Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

SPONSORS:  
University of Texas Health Science Center at Houston  
Prairie View A & M University

REGISTRATION:  
Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

TITLE: Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

DESCRIPTION: Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their

families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, other health care professionals, clergy, lawyers, medical, nursing, social work students, psychologists and IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

#### SOUTHEASTERN WORKSHOP

DATES: January 14 & 15, 1993

##### LOCATION:

Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

##### SPONSORS:

University of South Florida  
Florida A & M University

##### REGISTRATION:

Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

#### SOUTHWESTERN WORKSHOP

DATES: February 12 & 13, 1993

##### LOCATION:

Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

##### SPONSORS:

Arizona State University  
Northern Arizona University

##### REGISTRATION:

Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

TITLE: Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

DESCRIPTION: This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel

format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

For further information regarding these workshop or future NIH/FDA National Human Subject Protections Workshops, contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

##### BREEDING AND EXPERIMENTAL FACILITY FOR WOODCHUCKS (MARMOTA MONAX)

NIH GUIDE, Volume 21, Number 35, October 2, 1992

RFP: NIH-NIAID-DMID-93-10

P.T. 34; K.W. 1002002

National Institute of Allergy and Infectious Diseases

The Enteric Diseases Branch of the Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, has a requirement for the continued development and use of sequelae such as chronic hepatitis and hepatoma. There is a requirement for colony born animals for planned experiments. The contractor will be responsible for the development and maintenance of a colony of breeding *Marmota monax* capable of yielding 100 weaned pups per year; for the performance of experimental protocols on woodchucks with viral agents, vaccines, and therapeutic agents; and for the maintenance of experimental animals.

Request for Proposals (RFP) NIH-NIAID-DMID-93-10 is now available. Proposals will be due on November 13, 1992. It is anticipated that one cost-reimbursement, level-of-effort contract will be awarded for a period of five years.

To receive a copy of this RFP, please supply this office with two self-addressed mailing labels. All inquiries must be in writing and addressed to the office below:

Sara Southard  
Contract Specialist  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C07  
6003 Executive Boulevard  
Bethesda, MD 20892

All responsible sources may submit a proposal that will be considered by the government. This advertisement does not commit the government to award a contract.

##### FAMILY AND CHILD WELLBEING RESEARCH NETWORK

NIH GUIDE, Volume 21, Number 35, October 2, 1992

RFA AVAILABLE: HD-93-08

P.T. 34, AA; K.W. 0730010, 0730005

National Institute of Child Health and Human Development

Application Receipt Date: December 18, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

##### PURPOSE

The Demographic and Behavioral Sciences Branch of the Center for Population Research at the National Institute of Child Health and Human Development (NICHD) announces the availability of an RFA that invites applications for cooperative agreements (U01) to develop a research network to investigate the relationship of family factors to child welfare. The research network will conduct a systematic analysis of existing data to determine what can be learned by means of secondary data analysis about the relationship of family factors to child welfare.

Each investigator in the network will be expected to have demonstrated expertise and access to at least one data set relevant to the topic. Also, applicants must demonstrate that they have both the substantive and

statistical expertise to function as part of an interdisciplinary research network. Each investigator will be given support to pursue his or her individual research agenda, but a large part of the available resources will be held in reserve to address cooperative research questions agreed upon by the network. Each investigator will propose both an individual research plan and a cooperative research plan in which they identify areas of research that they would be willing to cooperate in implementing.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Family and Child Wellbeing Research Network, is related to the priority areas of family planning, educational and community-based programs, maternal and infant health, immunization and infectious diseases, and clinical preventive services. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

Institutions may submit applications on behalf of more than one Principal Investigator (PI), but each PI must submit a separate application.

#### MECHANISM OF SUPPORT

The funding mechanism to be used to support the research network will be the cooperative agreement (U01). Cooperative agreements are assistance mechanisms but differ from research project grants in that there will be substantial programmatic involvement of the NICHD Project Coordinator above and beyond the levels required for traditional program management of grants. Specifically, the Project Coordinator will assist the PI in the research network. All parties agree to accept the participatory and cooperative nature of the group process.

This RFA is intended as a one time solicitation. The total project period for the research network is five years and applications submitted in response to the present RFA must not request support for more than five years. Should there be a sufficient continuing program need, the NICHD may reissue this RFA. The anticipated award date is July 1, 1993.

#### FUNDS AVAILABLE

It is anticipated that up to seven awards will be made. \$1 million of direct cost support has been set aside to support the network for the first year of the award, and this amount will increase by an inflation factor in subsequent years of the network. Approximately one half of the resources allocated for the network will be devoted to support cooperative research. Resources available for cooperative research will be very small in the first year of the network, but will increase progressively in the subsequent years of the network. The percentage of funding for cooperative research will increase according to the following schedule: 20 percent in FY 93, 35 percent in FY 94, 50 percent in FY 95, 65 percent in FY 96 and 80 percent in FY 97. The level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program will be provided for in the financial plan of the NICHD, the award of grants pursuant to this RFA is also contingent on the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

There are a large number of social problems that impinge on the wellbeing of children. Among them, poverty and the emergence of an underclass population with a growing dependence on public transfer programs are highly visible areas of concern. Moreover, family factors such as marital instability, out-of-wedlock childbearing and changes in the demographic and economic structure of the family seem to be inextricably related to these and other problems affecting child wellbeing. It is important to describe fully these interconnections and to formulate and test models of the causes and consequences of these relationships. It is also important to elucidate the mechanisms of action by which family factors effect child wellbeing so that possible avenues of social intervention can be ascertained, and existing interventions, such as child support enforcement or child care subsidies, can be evaluated.

The American family has undergone considerable change in modern times. These changes are associated with changes in the way children are raised and with changes in familial support structures that sustain and develop children into productive adults. It is the intent of this RFA to measure both family factors and child wellbeing very broadly to develop as comprehensive a picture as possible about the relationship between these considerations. It is important to understand how family factors and socio-economic conditions combine to nurture children and help them develop into productive adults from both an individual and societal perspective. It is important to understand how the intergenerational structure of the family marshals resources to care for dependent children and how intergenerational family processes relate to public intervention to sustain and develop children.

The research network will confine its activity to secondary data analysis. The network will be assembled to achieve the broadest possible coverage in terms of research perspective, analytical technique and sources of data. The focus of the network is the United States, but the use of foreign data may be justified if it provides an important insight into the American condition. Investigators must demonstrate that they have a long term research agenda that is addressing important questions relevant to the research goals of this RFA. In addition they must describe the sources of data to which they have access and plan to use in their research plan. It is important to describe the extent to which the investigator has experience using these data. It



is also important to outline the analytic plan of attack and to describe the statistical techniques that will be employed in each phase of the research plan. The investigator must propose a plan of action necessary to accomplish their personal research agenda in this area. Applicants must also present a research plan for work they suggest for collaborative undertaking.

#### SPECIAL REQUIREMENTS

The cooperative agreement assistance mechanism imposes special requirements on both the applicants and the NICHD. These requirements are detailed clearly in the full RFA.

#### APPLICATION PROCEDURES

The grant application form PHS 398 (rev. 9/91) is to be used in applying for this grant. The PHS 398 is available from most business offices or grants/contracts offices at most institutions and can also be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. Applications must be received at the Division of Research Grants by December 18, 1992. If an application is received after that date, it will be returned to the applicant without review.

#### REVIEW CONSIDERATIONS

Those applications that are complete, responsive, and competitive will be evaluated in accordance with the criteria stated in the RFA announcement for scientific/technical merit by a special Review Committee convened by the NICHD. The second level of review will be provided by the National Child Health and Human Development Advisory Council.

#### AWARD CRITERIA

The anticipated date of award is July 1, 1993. An attempt will be made to balance the network so that it will have a multi-disciplinary composition, a diversity of research issues, and broad coverage of extant data sources. Awards will be made on the basis of the scientific merit of each research application and the need to create a balanced network.

#### INQUIRIES

It is essential to obtain a full version of this RFA before writing an application. Inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

To obtain a full version of the RFA or make inquiries regarding programmatic issues contact:

V. Jeffery Evans, Ph.D., J.D.  
Demographic and Behavioral Sciences Branch  
Center for Population Research  
National Institute of Child Health and Human Development  
6100 Executive Boulevard, Room 8B13  
Bethesda, MD 20892  
Telephone: (301) 496-1174  
FAX: (301) 496-0962

Direct inquiries regarding fiscal matters to:

Ms. Melinda Nelson  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North Building, Room 505  
Bethesda, MD 20892  
Telephone: (301) 496-5481  
FAX: (301) 402-0915

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.864. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations, 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency review.

## DIABETES ENDOCRINOLOGY RESEARCH CENTERS

NIH GUIDE, Volume 21, Number 35, October 2, 1992

RFA AVAILABLE: DK-93-01

P.T. 04; K.W. 0715075, 0785050, 0765020, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: December 14, 1992

Application Receipt Date: January 14, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

### PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites applications for funding of one Diabetes Endocrinology Research Center (DERC) grant to be competitively awarded in Fiscal Year 1994.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Diabetes Endocrinology Research Centers, is related to the priority area of diabetes mellitus. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Minority individuals and women are encouraged to submit as Principal Investigators. Foreign institutions are not eligible to apply.

### MECHANISM OF SUPPORT

Support of this program will be through the National Institutes of Health (NIH) grant-in-aid core center (P30) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. In addition to the requirements stated in the announcement, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement. The anticipated award date will be December 1, 1993.

### FUNDS AVAILABLE

The NIDDK anticipates awarding one DERC Grant in Fiscal Year 1994 on a competitive basis. The receipt of one competing continuation application is anticipated, which will be in competition with the other applications received in response to this announcement. The anticipated award will be for five years and will be contingent upon the availability of appropriated funds. Requests for support must be limited to no more than \$750,000 indirect costs per year. Any application exceeding this amount will be returned to the applicant.

### RESEARCH OBJECTIVES

The NIDDK-supported DERCs are part of an integrated program of diabetes-related research support provided by the NIDDK. These Centers have provided a focus for increasing collaboration and cost effectiveness among groups of successful investigators at institutions with established comprehensive diabetes research bases.

The objectives of the DERCs are to bring together investigators from relevant disciplines in a manner that will enhance and extend the effectiveness of research related to diabetes and its complications. Applicants should consult with NIDDK staff concerning plans for the development of the Center.

### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them. The study design must seek to identify any pertinent gender or minority differences.

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

### LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent by December 14, 1992. The letter of intent need only include a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number

and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDDK staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to the Chief, Review Branch, NIDDK at the address noted below.

#### APPLICATION PROCEDURES

Applications are to be submitted on the form PHS 398 (rev. 9/91), available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. On item 2a of the face page of the application, applicants must enter the RFA number and title.

Applicants are strongly encouraged to request a copy of "Guidelines for Diabetes Endocrinology Research Centers." These guidelines contain important additional information about the format, content, and review criteria. Prospective applicants may obtain guidelines from and may address inquiries to Dr. Garfield at the address listed under INQUIRIES.

Applications must be received by January 14, 1993. The original and three copies of the application must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Two additional copies of the application must be sent under separate cover to:

Review Branch  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 406  
Bethesda, MD 20892

#### REVIEW CONSIDERATIONS

Applications for a DERC grant will be evaluated by the NIH grant peer review process. Applications will be reviewed initially by an ad hoc review group convened by the NIDDK and subsequently by the National Diabetes and Digestive and Kidney Diseases Advisory Council.

#### Schedule

Letter of Intent Receipt Date:	December 14, 1992
Application Receipt Date:	January 14, 1993
Initial Review Dates:	Jun/Jul 1993
Second Level Review Date:	Sep/Oct 1993
Anticipated Award Date:	December 1, 1993

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. Direct inquiries regarding programmatic issues and requests to:

Dr. Sanford A. Garfield  
Diabetes Centers Program Director  
Division of Diabetes, Endocrinology, and Metabolic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 626  
Bethesda, MD 20892  
Telephone: (301) 496-7418  
FAX: (301) 480-038

Direct inquiries regarding fiscal matters to:

Ms. Linda Stecklein  
Team Leader and Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.847. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## GRANTS FOR HEALTH SERVICES DISSERTATION RESEARCH

NIH GUIDE, Volume 21, Number 35, October 2, 1992

RFA AVAILABLE: HS-93-01

P.T. 34; K.W. 0730050, 0710030

Agency for Health Care Policy and Research

Application Receipt Date: January 22, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

### PURPOSE

The Agency for Health Care Policy and Research (AHCPR) announces the availability of an RFA for grants for health services dissertation research. The AHCPR conducts research that will enhance the quality, appropriateness, and effectiveness of health care services, and access to such services. The provision of dissertation grant support is part of the effort of the AHCPR to stimulate the development of innovative and timely research on issues related to the delivery of health care services. Grant support is designed to aid the career development of new health services researchers and to encourage individuals from a variety of academic disciplines and programs to study complex issues with respect to health care services.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. The AHCPR urges applicants to submit grant applications with relevance to specific objectives of this initiative. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

A student applying for a dissertation research grant must be enrolled in an accredited doctoral degree program in the social, management, medical, or health sciences. The student also must be conducting or intending to conduct dissertation research on issues related to the delivery of health care services as described below. The proposed Principal Investigator (PI) must be a registered doctoral candidate in resident or nonresident status. All requirements for the doctoral degree other than the dissertation must be completed by the time of the award. This information must be verified in a letter of certification from the thesis chairperson and submitted with the grant application (see APPLICATION PROCEDURES).

The applicant may be either the institution that will administer the grant on behalf of the proposed PI or the proposed PI applying as an individual. Whenever feasible, the proposed PI is encouraged to have the application administered through an institution.

A proposed PI for dissertation research grant support need not be a U.S. citizen. However, a PI who is not a U.S. citizen and does not have a permanent resident visa must apply through an institution.

A PI who receives support for dissertation research under a grant from the AHCPR may not at the same time receive support under a predoctoral training grant or fellowship grant awarded by any other agency of the U.S. Department of Health and Human Services.

### MECHANISM OF SUPPORT

This RFA will use the AHCPR small grant (R03). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the proposed PI. In addition to the requirements stated in this RFA, awards will be administered under PHS grants policy as described in the PHS Grants Policy Statement. The budget of an application for a dissertation research grant must not exceed \$20,000 in total direct costs for the entire project period. An application that exceeds this amount will be returned to the applicant. Investigators may request support only for the amount of time necessary to complete the dissertation. A dissertation research grant usually is awarded for a period of 12 months or less but may be awarded for up to 17 months.

### FUNDS AVAILABLE

The AHCPR expects to fund about 15 to 20 dissertation research projects in 1993. The number of awards will depend on the availability of funds.

### RESEARCH OBJECTIVES

Only applications that propose studies in the areas identified in section 902 of the Public Health Service Act are eligible for support. Section 902 authorizes research in the following areas:

- o Effectiveness, efficiency, and quality of health care services
- o Outcomes of health care services and procedures
- o Clinical practice, including primary care and practice-oriented research
- o Health care technologies, facilities, and equipment



- o Health care costs, productivity, and market forces
- o Health promotion and disease prevention
- o Health statistics and epidemiology
- o Medical liability
- o AIDS/HIV infection
- o Rural health services
- o Health of low-income, minority, elderly, and other underserved populations

Applicants are encouraged to discuss the suitability of their research topics by letter or by phone with AHCPR staff members listed under INQUIRIES.

#### SPECIAL INSTRUCTIONS TO APPLICANTS CONCERNING INCLUSION OF WOMEN AND MINORITIES IN RESEARCH STUDY POPULATIONS

The AHCPR requires applicants for research grants to include minorities and women in study populations. If women or minorities are excluded or inadequately represented in research, a clear and compelling rationale should be provided. All applications for research submitted to the AHCPR are required to address this policy with respect to the inclusion of women and minorities. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants, in accordance with the special instructions described here and in the application kit. Research grant application materials, special instructions for dissertation grant applications, and the RFA are available from:

AHCPR Publications Clearinghouse  
P.O. Box 8549  
Silver Spring, MD 20907  
Telephone: 1-800-358-9295

Applications must be received by Friday, January 22, 1993, to Division of Research Grants, National Institutes of Health, Westwood Building, Room 240, Bethesda, MD 20892. A letter from the faculty committee or university official directly responsible for supervising the development and progress of the dissertation research must be submitted with the application. The letter must (1) fully identify the members of the committee and certify their approval of the dissertation proposal, (2) certify that all requirements for the doctoral degree except the dissertation are completed (or will be completed by the time for the grant award), and (3) note that the university official or faculty committee expects the doctoral candidate to proceed with the approved project proposal with or without AHCPR support.

#### REVIEW CONSIDERATIONS

Dissertation research grant applications will be reviewed under AHCPR review procedures by non-Federal experts, senior AHCPR staff members, and other experts in the Federal government. Reviewers will be selected on the basis of their health services research accomplishments and knowledge and their experience in research career development. Because reviews are rigorous, considerable methodological detail is important in the narrative of the application. All elements of the application will be considered in the review process. Primary emphasis will be given to the significance, scientific merit, and feasibility of the project.

Applications may be subject to triage to determine their scientific merit relative to other applications received in response to this RFA. The AHCPR will withdraw from further consideration those applications judged by triage to be noncompetitive for award and notify the PI and institutional official. Those applications judged to be competitive will undergo further scientific merit review. Review results and funding decisions will be announced approximately five months after the submission date. Review criteria, award criteria, and continuation of support are described below.

#### Review Criteria

Applications are reviewed to determine their suitability to review criteria in four major areas: problem significance, research design, investigator's qualifications and support structure, and budgetary appropriateness. Detailed criteria for these areas, as they relate to dissertation research, are provided in the RFA.

#### AWARD CRITERIA

Reviewers will provide recommendations with regard to the scientific and technical merit of the application and whether it should receive further consideration. Funding decisions are based on the recommendations of the reviewers, the relevance of the project to program priorities, and the availability of appropriated funds.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. Applicants are encouraged to discuss programmatic issues, such as the suitability of their research topics, by letter or telephone with:

Julius Pellegrino, M.B.A., M.P.H.  
Program Coordinator, Dissertation Grants  
Center for General Health Services Extramural Research  
Executive Office Center, Suite 502  
2101 E. Jefferson Street  
Rockville, MD 20852  
Telephone: (301) 227-8357

Direct inquiries regarding instructions for completing the application to:

Galen B. (Sandy) Warren, D.D.S., M.P.H.  
Office of Scientific Review  
Agency for Health Care Policy and Research  
Executive Office Center, Suite 602  
2101 E. Jefferson Street  
Rockville, MD 20852  
Telephone: (301) 227-8449

Direct inquiries regarding fiscal and administrative matters to:

Ralph Sloat  
Chief, Grants Management Branch  
Agency for Health Care Policy and Research  
Executive Office Center, Suite 601  
2101 E. Jefferson Street  
Rockville, MD 20852  
Telephone: (301) 227-8447

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.226. Awards are made under authority of title IX of the Public Health Service Act, as amended (42 U.S.C. 299-299c-6), and administered under PHS grants policies and in accordance with regulations of Title 42 of the Code of Federal Regulations, Part 67, Subpart A. The requirements of Executive Order 12372, Intergovernmental Review of Federal Programs, are not applicable to AHCPR research grant programs.

#### IMPROVING HYPERTENSIVE CARE FOR INNER CITY MINORITIES

NIH GUIDE, Volume 21, Number 35, October 2, 1992

RFA AVAILABLE: HL-93-02-P

P.T. 34; K.W. 0715115, 0414014, 0413001, 0403004, 0502017

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: November 30, 1992  
Application Receipt Date: February 16, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Epidemiology and Clinical Applications (DECA) invites applications for demonstration and education projects aimed at improvements in hypertensive care among inner city minority populations. The awards will be for a funding period of four years. The program will focus on community-based health education and/or other approaches for enhancing compliance and improving blood pressure control in urban minority populations. The intervention models should be widely applicable and economical. While hypertension is the focus of the program, a multiple risk factor approach may be used to assess changes in other cardiovascular risk factors.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Improving Hypertensive Care for Inner City Minorities, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign organizations are not eligible to apply and domestic applications may not include international components. Applications from minority individuals, particularly African Americans and Hispanics, and women are encouraged.

#### MECHANISM OF SUPPORT

The support mechanism for this RFA will be the National Institutes of Health (NIH) demonstration and education (D&E) research grant (R18). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed four years. The anticipated award date is September 30, 1993.

## FUNDS AVAILABLE

It is anticipated that three to five centers will be supported over the four year period of this program. An estimated total cost (direct and indirect) of \$2,500,000 will be available for the first year of funding for the entire program, with an estimated four year total cost of \$10,600,000. This level of support is dependent upon the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Heart, Lung, and Blood Institute (NHLBI), awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

The primary objective of this four-year demonstration and education research program is to develop, and to evaluate for feasibility, acceptability, and effectiveness, methods to maintain therapy and control of hypertension, for both newly and previously diagnosed individuals, in inner city, primarily minority populations. The focus will be on community-based health education and other approaches for enhancing compliance and improving blood pressure control among inner city minority populations. The delivery of and adherence to the interventions is the main objective, rather than clinical algorithms used to treat hypertension. While the improvement of hypertensive care is the focus of this program, other cardiovascular disease risk factors may be included in the interventions, and changes in these factors should be assessed. The role of non-pharmacologic approaches to reducing blood pressure, including drug and alcohol avoidance, should be addressed.

Primary outcome measures to assess the interventions may include: percentages aware of hypertension, screened for hypertension, treated for hypertension, responding to treatment, and controlled to normal levels of blood pressure; clinic attendance; and compliance with therapy. Secondary outcomes include the assessment of: effects on other CVD risk factors, e.g., cigarette smoking, overweight, lipid profile, and diabetes; health quality of life measures; and cost effectiveness of the interventions.

The experimental design is not restricted by this RFA. Applicants should develop their own independent design, and provide justification for the proposed design. The designs should focus on an integrated approach including various management factors that have previously been shown to be effective. Health education and other approaches for enhancing compliance and improving blood pressure control should be adequately described. A randomized design, comparing special interventions against usual care would be one appropriate study design to test intervention models. If justified by the nature of the proposed intervention, i.e., delivery of an intervention to a social group (e.g., neighborhood or employee group), other designs will be considered responsive.

Annual meetings, to be held in Bethesda, MD, are planned for the exchange of information among investigators. Applicants must budget the travel costs associated with these meetings in their applications.

## STUDY POPULATIONS

Because of their excess burden of hypertension, African Americans should comprise a large proportion of the study population. Although there is no compelling evidence of excess burden from hypertension among Hispanics compared to the population at large, socioeconomic factors for inner-city members of this group may result in less than optimal hypertension detection and treatment. Therefore, the inclusion of Hispanics, which may be best accomplished by the inclusion of Hispanics as the majority of the sample at one of the study sites, may be proposed. Investigators should also consider other minority groups, as well as low socioeconomic whites, for inclusion. The inclusion of low socioeconomic-status (SES) whites may provide some means to separate the effects of SES and ethnicity. As the lowest hypertension control rates are seen in young African Americans, investigators should address the advantages and disadvantages of oversampling this younger segment of the population.

## SPECIAL INSTRUCTIONS TO FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women and minorities are not included in the study populations for clinical studies, specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by November 30, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NHLBI staff to estimate the potential workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

C. James Scheirer, Ph.D.  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 548  
Bethesda, MD 20892  
Telephone: (301) 496-7363  
FAX: (301) 402-1660



## APPLICATION PROCEDURES

The research grant application form 398 (rev. 9/91) is to be used in applying for this award. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441; and from the NHLBI Program Administrator named below.

Applications must be received by February 16, 1993. If an application is received after that date, it will be returned to the applicant. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NHLBI staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications that are found to be responsive will be reviewed for scientific and technical merit by an initial review group, convened by the Division of Extramural Affairs, NHLBI solely to review these applications. The initial review will include an evaluation to determine scientific merit relative to other applications received in response to this RFA. The NIH will withdraw from further competition those applications judged non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will be further evaluated for scientific/technical merit by the usual peer review procedures, including, if deemed appropriate, a reverse site visit at the applicant's expense. Secondary review of applications will be conducted by the National Heart, Lung, and Blood Advisory Council.

## AWARD CRITERIA

Applications recommended by the National Heart, Lung, and Blood Advisory Council will be considered for award based upon scientific and technical merit, overall program balance, and the availability of funds. The anticipated date of award is September 30, 1993.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

P. Scott Allender, M.D.  
Prevention and Demonstration Research Branch  
Division of Epidemiology and Clinical Applications  
National Heart, Lung, and Blood Institute  
Federal Building, Room 604  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-2465

Direct inquiries regarding fiscal matters to:

William W. Darby  
Section Chief, Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A11  
Bethesda, MD 20892  
Telephone: (301) 496-7536

## AUTHORITY AND REGULATIONS

This project is described in the Catalog of Federal Domestic Assistance No. 93.837. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This project is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.



## ONGOING PROGRAM ANNOUNCEMENTS

### CHEMORECEPTION AND NUTRITION

NIH GUIDE, Volume 21, Number 35, October 2, 1992

PA NUMBER: TPA-93-009

P.T. 34; K.W. 0710095, 1002004, 0705070

National Institute on Deafness and Other Communication Disorders  
National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute of Dental Research  
National Institute on Aging  
National Institute of Child Health and Human Development

#### PURPOSE

The purpose of this Program Announcement (PA) is to foster basic and clinical research on the interactions between chemoreception and nutrition. This research may involve the effects of nutritional variables on taste, smell, and somatosensory chemoreception, or this research may involve the effects of chemosensory variables on nutrition and diet.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Chemoreception and Nutrition, is related to the priority area of nutrition. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) Award (R29).

#### MECHANISM OF SUPPORT

The mechanisms available for the support of this program are research project grants (R01) and the FIRST Award (R29).

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources (NCRR) may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator must be included with the application.

#### RESEARCH OBJECTIVES

The support of nutrition research at the National Institutes of Health (NIH) includes studies designed to assess the consequences of food or nutrient intake and utilization in the intact organism, including humans, and the metabolic and behavioral mechanisms involved. These studies encompass investigation of nutrient variables at the cellular or subcellular level. These studies also include investigations of genetic/ environmental interactions in which a nutrient is a variable and dietary practices are expected to produce changes in health status, including the maintenance of health and the treatment of disease in humans. Current research in nutrition at the NIH is periodically reported in the Nutrition Coordinating Committee's publication entitled "Nutrition Research at the NIH," which includes examples of nutrition-related chemosensory research supported by the NIH. Potential applicants may obtain a copy of "Nutrition Research at the NIH" (NIH Publication No. 91-2611) through the Division of Research Coordination, Building 31, Room 4B63, Bethesda, MD 20892 (telephone 301-496-4982).

The goal of this PA is to foster basic and clinical research that will lead to a better understanding of the interactions between chemoreception and nutrition and better preventive interventions for chemosensory and nutritional disorders. This research may involve the effects of nutritional variables on chemoreception, including taste, smell, and somatosensory responses related to oral and nasal chemoreception; this research may also be focused on the effects of chemosensory variables on nutrition and diet. A broad range of studies covering the molecular to the behavioral levels of research is encouraged. Interactions among investigators in various biomedical and behavioral fields and disciplines are encouraged, including nutrition, psychophysics, biochemistry, and molecular biology.

Research topics might include those below. Investigators are encouraged to consider other topics relevant to this program.

o Nutritional influences, including excessive nutrient intake, on the molecular structure and function of chemosensory epithelia and on secretory transport and other perireceptor events related to chemoreception, including mucosal defense mechanisms.

- o Alteration of chemosensory receptor membrane events, including the modification of sweet, bitter, sour, and salt taste sensation, by influencing receptor binding or second messenger activation.
- o Nutritional influences on the regeneration cycle of olfactory receptor neurons and taste bud cells under normal physiological conditions and after injury to the chemosensory systems.
- o Effects of dietary alterations in early life on the structure and function of chemosensory systems, including trigeminal chemoreception; effects of dietary alterations in early life on the development of sweet, bitter, sour, and salty taste and amiloride-sensitive sodium channels.
- o Mother-infant relationships involving odors and nutrition.
- o Relation of smell, taste, and somatosensory aspects of flavor perception to the amount of food consumed and the types of foods selected and rejected.
- o Genetic studies involving food preferences and individual differences in chemosensory abilities, for example, the ability to taste phenylthiourea and other bitter substances and to smell androstenone; studies of patients with Kallmann's disease or familial dysautonomia.
- o Associations between chemosensory disorders and altered food intake in age-related conditions and various chronic disease states, including oral and dental diseases (e.g., xerostomia, dental caries, and periodontal disease), obesity, diabetes, inborn errors of metabolism, and digestive, hepatic, and kidney diseases.
- o Effects of artificial sweeteners and salt substitutes on nutrition and chemoreception.
- o Nutritional and chemosensory status in special subpopulations, including minorities, nursing mothers, and postmenopausal women with burning mouth symptoms; individuals with pseudohypoparathyroidism associated with G protein deficiency and hyposmia; those receiving hormonal therapy.
- o Iatrogenic alterations of nutritional and chemosensory status resulting from interventions, such as oral and dental prosthesis, hemodialysis, irradiation, and chemotherapy.
- o Impact of the affective dimensions of chemoreception in health and disease on food choices and utilization; impact of depressive and eating disorders on chemosensory affect and sensitivity; impact of dysosmia and dysgeusia on food choices and intake.
- o Role of chemoreception in digestion and metabolism of nutrients.
- o Development of chemosensory test stimuli that mimic chemosensory properties of food and permit stimulus control.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS.

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants/offers are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be

considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in line 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by an appropriate National Advisory Council or Board.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Program balance among research areas of the announcement
- o Availability of funds

#### INQUIRIES

Direct inquiries regarding the major areas of research interest in this nutrition program to:

##### Chemoreception

Rochelle Small, Ph.D.  
Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-3464  
FAX: (301) 402-6251

##### Obesity and Nutrition Sciences

Van S. Hubbard, M.D., Ph.D.  
Director, Obesity, Eating Disorders and Energy Regulation  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A18  
Bethesda, MD 20892  
Telephone: (301) 496-7823  
FAX: (301) 402-1278

##### Oral Diseases and Conditions

Joseph E. Ciardi, Ph.D.  
Director, Caries, Nutrition and Fluoride Program  
Extramural Programs  
National Institute of Dental Research  
Westwood Building, Room 509  
Bethesda, MD 20892  
Telephone: (301) 496-7784  
FAX: (301) 496-4180

## Aging

Ann Sorenson, Ph.D.  
Biology of Aging Program  
National Institute on Aging  
Gateway Building, Room 2C231  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-6402  
FAX: (301) 402-0010

## Development

Ephraim Y. Levin, M.D.  
Medical Officer, Endocrinology, Nutrition and Growth Branch  
Center for Research for Mothers and Children  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 637  
Bethesda, MD 20892  
Telephone: (301) 496-5593  
FAX: (301) 402-2085

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Grants Management Branch  
Division of Extramural Activities  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
Rockville, MD 20892  
Telephone: (301) 402-0909  
FAX: (301) 402-1758

Paulette Badman  
Grants Management Specialist  
Division of Extramural Programs  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 637  
Bethesda, MD 20892  
Telephone: (301) 496-7467  
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Theresa Ringler  
Chief, Grants Management Section  
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Westwood Building, Room 518  
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FAX: (301) 402-1260

Mary Daley  
Grants Management Branch  
National Institute on Aging  
Gateway Building, Room 2N212  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-1472  
FAX: (301) 402-0066

Edgar Douglas Shawver  
Chief, Maternal and Child Research Grants Management Section  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 505  
Rockville, MD 20892  
Telephone: (301) 496-1303  
FAX: (301) 402-0915

## AUTHORITY AND REGULATIONS

The programs of the National Institute on Deafness and Other Communication Disorders, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Dental Research, National Institute on Aging, and National Institute of Child Health and Human Development, are identified in the Catalog of Federal Domestic Assistance, Nos. 93.173, 93.848, 93.121, 93.866 and 93.865, respectively. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.



## PREVENTION OF END STAGE LIVER DISEASES BY MOLECULAR DIAGNOSIS

NIH GUIDE, Volume 21, Number 35, October 2, 1992

PA NUMBER: TPA-93-010

P.T. 34; K.W. 0745020, 1002008, 1002019

National Institute of Diabetes and Digestive and Kidney Diseases

### PURPOSE

The purpose of this Program Announcement (PA) is to encourage research on isolating the gene(s) or the full length cDNAs for the gene(s) of the many genetic liver diseases in which early diagnosis and treatment could avert progressive serious liver injury. Liver transplantation is often the only treatment for these diseases when they are not detected and treated early. Two of the liver diseases in which early diagnosis could be curative and in which much information exists about the gene and/or its location are Wilson's disease and hemochromatosis.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Prevention of End Stage Liver Diseases by Molecular diagnosis, is related to the priority area of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit United States organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29).

### MECHANISM OF SUPPORT

The Research Project Grant (R01), the FIRST Award (R29), and the Interactive Research Project Grant (interactive R01s) are all appropriate mechanisms. Program Project Grant (P01) or Center Grant (P30) applications will not be accepted.

### RESEARCH OBJECTIVES

Hemochromatosis and Wilson's disease are two inherited diseases of trace metal metabolism that can cause end stage liver disease. If diagnosed early before the onset of significant liver damage, available treatments are usually effective. Unfortunately, both hemochromatosis and Wilson's disease are rarely diagnosed before the onset of symptoms in the liver or other organs. Both diseases result in liver cirrhosis for which liver transplantation is the only effective treatment. Currently, there is no easy means of early screening for either disease since the genetic defect has not been positively identified.

Hemochromatosis, which affects approximately one in 300 persons, appears to be due to an excessive absorption of dietary iron that leads over years to excessive bodily iron stores that eventually cause cellular damage and organ injury in liver, heart, pancreas and gonads. If hemochromatosis is diagnosed, the organ injuries can be averted by phlebotomy to decrease the body iron stores to normal. The enzyme or transport protein responsible for the excessive absorption of iron has not been identified. It is not ferritin, transferrin, or the transferrin receptor. The new techniques of molecular biology promise to provide means of identifying the defect in hemochromatosis. The molecular techniques needed are probably not the conventional ones that proceed from the abnormal protein to the gene, but rather "reverse genetics" that first identifies the gene and from it the abnormal protein. Such techniques were successful in identifying the abnormality in cystic fibrosis and neurofibromatosis. Indeed, in hemochromatosis an advantage has been established already by the known linkage of this disorder with the HLA region on the short arm of chromosome 6. If the gene for hemochromatosis could be identified, genetic screening of newborns could be used to identify homozygotes and to initiate lifelong phlebotomy therapy before the onset of disease or organ damage.

Wilson's disease, which affects approximately one in 10,000 persons, appears to be due to a genetic defect in the secretion of copper in bile that leads over time to a gradual accumulation of excessive copper stores in the liver, red blood cells, synovium, kidneys and brain. Untreated Wilson's disease leads to irreversible end stage liver disease and/or brain damage between the ages of 15 and 40 years. If Wilson's disease can be identified early, however, the copper accumulation can be prevented by chelation therapy (d-penicillamine) and the liver and brain disease completely averted. Unfortunately, Wilson's disease is rarely diagnosed early, and this is still an important cause of liver failure necessitating liver transplantation. Approaches that might be taken to identify the Wilson's disease gene also include those of reverse genetics by identifying genetic markers that co-segregate with this disease. Such studies require data collected from large families with Wilson's disease using multiple genetic markers. These studies have shown that this gene is located on chromosome 3. Further studies are needed to more closely locate the gene to a fragment of DNA that can be sequenced and characterized.

Both of these examples of diseases that could benefit from appropriate early diagnosis through molecular biology techniques require the availability of large family cohorts to serve as subjects and controls. The availability

of multi-generational families in which linkage analyses can be done will be very important to progress in these studies.

Other liver diseases such as Alagille syndrome and Crigler-Najjar syndrome type I, in which early diagnosis may make available treatment(s) that can prevent serious liver malfunction, may also be submitted and be responsive to this PA. The emphasis in this announcement is on the diagnosis of the genetic defect and not on the treatment of the disease.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them, and the study design must seek to identify any pertinent gender or minority population differences.

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the regular application deadlines as indicated in the application kit.

FIRST (R29) Award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award applications submitted without the required number of reference letters will be considered incomplete and will be returned to the applicant without review.

Application kits are available at most institutional business and grant/contract offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7447. The title and number of this announcement must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building Room 240  
Bethesda, MD 20892\*\*

## REVIEW CONSIDERATIONS

Applications will be assigned to initial review groups and to Institutes or Centers for possible funding on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by initial review groups of the Division of Research Grants in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by an appropriate National Advisory Council.

## AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Inquiries regarding programmatic issues may be directed to:

Sarah C. Kalser, Ph.D.  
Liver and Biliary Diseases Program Director  
Division of Digestive Diseases and Nutrition  
National Institute of Diabetes and Digestive and Kidney Diseases  
5333 Westbard Avenue, Room 3A-05  
Bethesda, MD 20892  
Telephone: (301) 496-7858

David G. Badman, Ph.D.  
Hematology Program Director  
Division of Kidney, Urologic, and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
5333 Westbard Avenue, Room 3A-05  
Bethesda, MD 20892  
Telephone: (301) 496-7458

Direct inquiries regarding fiscal matters to:

Miss Aretina Perry  
Grants Management Branch  
National Institute of Diabetes and Digestive and Kidney Diseases  
Bethesda, MD 20892  
Telephone: (301) 496-7467

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.848. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## RESEARCH INFRASTRUCTURE SUPPORT PROGRAM

NIH GUIDE, Volume 21, Number 35, October 2, 1992

PA AVAILABLE: MH-92-111

P.T. 14; K.W. 0715129, 0785035, 0710030

National Institute of Mental Health

THE PROGRAM ANNOUNCEMENT (PA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE PROGRAM ANNOUNCEMENT FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The National Institute of Mental Health (NIMH) is committed to expanding the number of institutions capable of supporting state-of-the-art clinical and services research and thus increasing the number of investigators obtaining extramural funding for their research. Expansion of the clinical research infrastructure is a major priority of the NIMH; the Research Infrastructure Support Program (RISP) is a direct response of the NIMH to recommendations made by the National Advisory Mental Health Council and by the NIMH Extramural Science Advisory Board. The purpose of this PA is to stimulate the development of new resources at institutions capable of developing and maintaining programs of clinical and services research directed at the major mental disorders.



The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. The PA, Research Infrastructure Support Program, is related to the priority areas of mental health and mental disorders. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by public and private, non-profit and for-profit organizations such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government, except for those institutions with NIMH research support exceeding \$3,000,000 (in total costs) in fiscal year 1991. Women and minorities are encouraged to apply.

#### MECHANISM OF SUPPORT

Grants awarded in the RISP program will use the Resource-Related Research Project mechanism (R24) to contribute to the improvement of the capability of resources to serve biomedical research.

#### RESEARCH OBJECTIVES

Many institutions with access to large and varied populations of individuals with mental disorders are not able to launch research programs because of limited technical and scientific support available within their research environment. This program will assist in the development of these and other resources that will form part of the institution's clinical research infrastructure.

Applicant institutions must describe a comprehensive and coherent plan of improvement to the institution's current research environment that will expand the capacity of investigators at the institution to carry out extramurally supported mental health research. The plan must have a focus on particular mental health clinical populations or diagnostic groups and must demonstrate accessibility of the population to institution-based investigators. The plan must also demonstrate the actual commitment of institutional resources which may include senior faculty release time, support staff, research bed costs, equipment costs assumed by the institution, and waiver of overhead costs.

A central philosophical principle underlying this program is that different institutions will require different types of infrastructure development activities and initiatives. Therefore, this announcement does not prescribe in any detail the nature of the activities to be applied for or supported.

The following types of support may be requested under this program:

- o Partial salary support for junior faculty, particularly women and minorities
- o Training expenses for junior faculty
- o Research patient recruitment, diagnosis, assessment, and follow-up
- o Clinical and scientific consultation, including expenses incurred by an external review and scientific advisory committee
- o Biostatistical and data-base management services
- o Small equipment and research instruments
- o Research technicians and assistants
- o Developmental, feasibility, or pilot studies

#### STUDY POPULATIONS

#### NIH POLICY CONCERNING INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

Applications for grants and cooperative agreements and proposals for contracts that involve human subjects are required to include minorities and both genders in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages. If one gender and/or minorities are excluded or are inadequately represented in this research, particularly in proposed population-based studies, a clear compelling rationale for exclusion or inadequate representation should be provided. The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., American Indians or Alaskan Natives, Asians or Pacific Islanders, Blacks, Hispanics). Investigators must provide the rationale for studies on single minority population groups.



The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applications for support of research involving human subjects must employ a study design with minority and/or gender representation (by age distribution, risk factors, incidence/prevalence, etc.) appropriate to the scientific objectives of the research. It is not an automatic requirement for the study design to provide statistical power to answer the questions posed for men and women and racial/ethnic groups separately; however, whenever there are scientific reasons to anticipate differences between men and women, and racial/ethnic groups, with regard to the hypothesis under investigation, applicants should include an evaluation of these gender and minority group differences in the proposed study. If adequate inclusion of one gender and/or minorities is impossible or inappropriate with respect to the purpose of the research, because of the health of the subjects, or other reasons, or if in the only study population available, there is a disproportionate representation of one gender or minority/majority group, the rationale for the study population must be well explained and justified.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants that do not comply with these policies.

#### APPLICATION PROCEDURES

Applicants are to use the research grant application form PHS 398 (rev. 9/91) in applying for these grants. The number and title of this PA, Research Infrastructure Support Program, must be typed in item 2a on the face page of the PHS application form.

Applications kits containing the necessary forms and instructions may be obtained from business offices and offices of sponsored research at most universities, colleges, medical schools, and other major research facilities. If such a source is not available, the necessary application materials may be obtained from the Grants Management Branch, National Institute of Mental Health, 5600 Fishers Lane, Room 7C-05, Rockville, MD 20857 (telephone 301/443-4414).

The signed original and five legible copies of the completed application must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by an initial review group (IRG) composed of primarily non-Federal scientific experts. Final review is by the appropriate National Advisory Council, review by Council may be based on policy considerations as well as scientific merit. By law, only applications recommended by the Council may be considered for funding. Summary statements of IRG discussions are sent to applicants as soon as possible following IRG review.

##### Review Criteria

- o Past research training record for both the program and the designated preceptors in terms of the rate at which former trainees establish independent and productive research careers
- o Past research training record in terms of the success of former trainees in obtaining individual awards such as fellowships, career awards, and research grants for further development
- o Objectives, design, and direction of the research training program
- o Caliber of preceptors as researchers including successful competition for research support
- o Training environment including the institutional commitment, the quality of the facilities, and the availability of research support
- o Recruitment and selection plans for appointees and the availability of high quality candidates
- o The record of the research training program in retaining health-professional post-doctoral trainees for at least two years in research training or other research activities
- o When appropriate, the concomitant training of health-professional post-doctorates (e.g., individuals with the M.D., D.O., D.D.S.) with basic science post-doctorates (e.g., individuals with a Ph.D., Sc.D.) will receive special consideration

Following scientific-technical review, the application will receive a second-level review by the appropriate National Advisory Council.

#### AWARD CRITERIA

Applications recommended for approval by the appropriate National Advisory Council will be considered for funding on the basis of overall scientific and technical merit of the research as determined by peer review, program needs and balance, and availability of funds.

## INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Grayson S. Norquist, M.D., M.S.P.H.  
Deputy Director, Division of Epidemiology and Services Research  
National Institute of Mental Health  
Parklawn Building, Room 18C-26  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-3683



Direct inquiries regarding fiscal matters to:

Stephen J. Hudak  
Chief, Grants Management Section  
National Institute of Mental Health  
Parklawn Building, Room 7C-23  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (301) 443-4456

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.3. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78- 410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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## For Grants and Contracts

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**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 36  
October 9, 1992

RICHARD W. MURPHY

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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\*\*81350E\*\*

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*



## NOTICES

### HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 36, October 9, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

#### **SOUTHWESTERN WORKSHOP**

**DATES:** November 16 & 17, 1992

**LOCATION:**

Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

**SPONSORS:**

University of Texas Health Science Center at Houston  
Prairie View A & M University

**REGISTRATION:**

Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

**TITLE:** Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

**DESCRIPTION:** Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, other health care professionals, clergy, lawyers, medical, nursing, social work students, psychologists and IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

#### **SOUTHEASTERN WORKSHOP**

**DATES:** January 14 & 15, 1993

**LOCATION:**

Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

**SPONSORS:**

University of South Florida  
Florida A & M University

**REGISTRATION:**

Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

**TITLE:** Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

#### SOUTHWESTERN WORKSHOP

DATES: February 12 & 13, 1993

#### LOCATION:

Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

#### SPONSORS:

Arizona State University  
Northern Arizona University

#### REGISTRATION:

Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

TITLE: Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

DESCRIPTION: This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

For further information regarding these workshop or future NIH/FDA National Human Subject Protections Workshops, contact:

Ms. Darlene Marie Ross  
Executive Assistant for Education  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
9000 Rockville Pike  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

#### REVISED PHS 416-9 APPLICATION FORM

NIH GUIDE, Volume 21, Number 36, October 9, 1992

P.T. 34; K.W. 1014006

Division of Research Grants

The Public Health Service (PHS) started mailing the revised Application for Public Health Service Individual National Research Service Continuation Award---PHS 416-9---to appropriate awardees in September 1992. This revision, dated 10/91, approved through 10/31/94, replaces the version that was revised 7/88 and approved through 4/30/91.

The major changes in the revised continuation award application include:

- o an explanation of the required documentation regarding gender and minority representation in study populations, and

o a new Checklist, form page 4, with an updated list of required assurances and certifications.

The PHS mails the 416-9 application kits directly to individual awardees several weeks before the due date. Thus, sponsoring institutions need not stock the form.

#### INQUIRIES

Questions about the monthly mailings of applications kits may be directed to:

Renewal Unit, Project Control Section  
Division of Research Grants  
Westwood Building, Room 253  
Bethesda MD 20892  
Telephone: (301) 496-7210

General questions regarding the use of the PHS 416-9 application may be directed to the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, telephone: (301) 496-7441 or the grants management specialist at the appropriate awarding institute or center of the PHS.

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

##### EVALUATION OF THE EFFECT OF A FAT MODIFIED DIET ON HORMONES DURING ADOLESCENCE

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFP AVAILABLE: NCI-CN-25502-51

P.T. 34, AA; K.W. 0710095, 0765025, 0760025

National Cancer Institute

The National Cancer Institute (NCI), Prevention and Control Contracts Section (PCCS), intends to issue a Request for Proposal (RFP) NCI-CN-25502-51. The Division of Cancer Prevention and Control, NCI, is conducting a study to evaluate the effect of a fat-modified diet on hormones during childhood and adolescence. The study is being performed ancillary to the Diet Intervention Study in Children (DISC), a randomized clinical trial sponsored by the Division of Epidemiology and Clinical Applications, National Heart, Lung and Blood Institute (NHLBI). The objectives of DISC are to determine whether a fat-modified diet during childhood and adolescence will lower LDL-cholesterol and to assess the feasibility and safety of this diet. The objectives of the NCI ancillary study are to evaluate the effect of this fat-modified diet on sex hormones and to correlate characteristics of children and adolescents, such as age, Tanner stage, anthropometry, diet, and physical activity, with sex hormone levels. This solicitation seeks a contractor to store serum specimens collected for DISC, develop and issue an RFP for a laboratory to perform serum hormone assays, evaluate the offerors' proposals, award a subcontract to the best qualified laboratory offering the best buy for the Government, and monitor the laboratory to ensure high quality work and fulfillment of contractual obligations. This RFP will be available on or about October 2, 1992, with responses due approximately six weeks thereafter. No collect calls will be accepted.

Copies of the RFP may be obtained by sending a written request to:

Christine L. Ptak, Contract Specialist  
Research Contracts Branch, PCCS  
National Cancer Institute  
Executive Plaza South, Room 635  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-8603

##### CULTURED NEURON PROBE

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFP AVAILABLE: NIH-NINDS-93-02

P.T. 34; K.W. 0740050, 0710085, 0750005, 0706000

National Institute of Neurological Disorders and Stroke

The Neural Prosthesis Program of the National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health, is seeking a contract to determine the feasibility of establishing connections with specific target neuronal populations in the mammalian central nervous system (CNS) by developing and evaluating a cultured neuron probe. If successful, the probes will be implanted into a mammalian CNS region and an attempt will be made to demonstrate two-way communication between the linking neurons and the target neurons. Personnel with established expertise in neurophysiology, biomaterials, and microfabrication are required. It is anticipated that one award will be made in May 1993, for a period of three years.

This is not a Request for Proposals (RFP). To receive a copy of the RFP, please submit a written request to the following address, and supply this office with two self addressed mailing labels. All responsible sources will be considered by the agency. The RFP will be issued on or about October 8, 1992 with proposals due on December 7, 1992.

Contracting Officer  
Contracts Management Branch, DEA  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 901  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Attention: RFP No. NIH-NINDS-93-02

**ANTIGENIC VARIATION OF HIV-1 AND RELATED LENTIVIRUSES**

**NIH GUIDE**, Volume 21, Number 36, October 9, 1992

RFP AVAILABLE: NIH-NIAID-DAIDS-93-13

P.T. 34; K.W. 1002045, 0710070, 0755010, 0780005

National Institute of Allergy and Infectious Diseases

The Vaccine Research and Development Branch, Basic Research and Development Program, Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID) has a requirement for a contractor to receive and process virus-infected, human-derived samples on a large scale basis and to isolate, expand and immunologically characterize HIV-1 and related lentiviruses from these samples. Specifically, the selected contractor will be responsible for: 1) performing virus isolation, expansion, and characterization from samples supplied to the Contractor; 2) performing specific immunological assays for HIV and related lentiviruses; 3) classifying all virus isolates received into antigenic subgroups based upon serological/immunological assays; 4) securing, receiving, cataloging, processing, and storing samples from both domestic and international sites, and distributing samples to other investigators; 5) providing inventory and a Database Management System; 6) providing facilities and resources; 7) reporting progress according to reporting requirements; 8) meeting with the Project Officer; 9) obtaining clearance for publication; and 10) implementing an orderly transition to a successor Contractor. This is an announcement for an anticipated Request for Proposals (RFP). RFP NIH-NIAID-DAIDS-93-13 will be issued on or about October 9, 1992 with a closing date tentatively set for December 22, 1992. One contract will be awarded as a result of this solicitation. It is expected that the contract will have a five-year period of performance. A level-of-effort cost-reimbursement contract is anticipated. Requests for the RFP shall be directed in writing to:

Chief, Contract Management  
Branch, National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C07  
Bethesda, MD 20892  
FAX: (301) 402-0972

Please provide this office with three self-addressed mailing labels. Telephone inquiries will not be honored and all inquiries must be in writing. A short-form version of the RFP will be provided first. That version includes only the statement of work and the Evaluation Criteria to be used for selection of the awardee. After examining this, a full-text version of the RFP must be requested, in writing for those offerors interested in responding. FAX requests are acceptable for the full-text version only. All proposals from responsible sources will be considered by the NIAID. This advertisement does not commit the Government to award a contract.

**PAPILLOMAVIRUS IN VITRO CELL CULTURE SYSTEMS**

**NIH GUIDE**, Volume 21, Number 36, October 9, 1992

RFA AVAILABLE: AI-92-08

P.T. 34; K.W. 1002045, 0780015, 0740020

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: November 6, 1992  
Application Receipt Date: December 10, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

**PURPOSE**

The Antiviral Research Branch of the Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases (NIAID), invites Cooperative Agreement applications from organizational entities willing to participate, with the assistance of the NIAID, in furthering innovative in vitro approaches to the study of papillomavirus infections and their therapeutic control. The research goals of this solicitation are to stimulate the use of in vitro papillomavirus replication systems for research on (1) the events of papillomavirus replication and pathogenesis; and (2) the antiviral potential of experimental therapeutic agents.

**HEALTHY PEOPLE 2000**

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Papillomavirus in Vitro Cell Culture Systems, is related to the priority area of sexually transmitted diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783- 3238).



## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

The funding mechanism to be used is the cooperative agreement (U01). The cooperative agreement differs from the traditional research grant in that there will be substantial programmatic involvement of NIAID staff above and beyond the levels required for traditional program management of grants. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary NIH peer review procedures.

## FUNDS AVAILABLE

It is expected that at least one application will be funded for a four-year period, contingent upon the receipt of a sufficient number of meritorious applications. It is expected that the total direct costs for the first year for successful applications will be around \$175,000. However, individual awards may be higher or lower.

## RESEARCH OBJECTIVES

Papillomavirus infection is a rapidly increasingly serious clinical problem in the United States and around the world. None of the currently available therapies has acceptable efficacy. The failure to develop a safe and effective therapy for these infections is due, in part, to the inability to replicate virus in vitro. In the past few years, several research groups have developed in vitro systems in which many of the events of papillomavirus replication have been reported to occur. The availability of these systems provides an unparalleled opportunity to investigate the mechanisms of papillomavirus replication and pathogenesis at a molecular level. This basic research may also result in the identification of viral genes which are promising targets for therapeutic intervention. In addition, these systems should provide a means to evaluate the potential anti-papillomavirus activity of experimental agents and provide a rational basis for selecting agents whose activity warrants further study in the animal models. The proposed systems may utilize either a human papillomavirus (HPV) or an animal papillomavirus as a model of HPV infection.

## Review Procedures

A preliminary review will be done by NIAID staff upon receipt of the applications. Any application that is incomplete or judged to be unresponsive to this RFA will be returned to the applicant without technical review. Applications that are complete and responsive may be subjected to a triage procedure by peer review to determine competitiveness among the applications. Applications judged to be competitive for award will be reviewed in detail in accordance with established NIH peer review procedures, by a special review committee convened specifically for this purpose by the Division of Extramural Activities, NIAID. This will be followed by a second-level review by the National Advisory Allergy and Infectious Diseases Council in June 1993.

## LETTER OF INTENT

Prospective applicants are asked to submit, by November 6, 1992, a letter of intent that includes a descriptive title of the proposed research, and the names and affiliation(s) of proposed key investigators. The NIAID requests a letter of intent in order to provide an indication of the number and scope of applications to be received. The letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application. The letter of intent will not enter into the review of any application subsequently submitted.

The letter of intent is to be sent to:

Dr. Olivia Preble  
Chief, Microbiology and Immunology Review Section  
Scientific Review Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C20  
6003 Executive Boulevard  
Rockville, MD 20892

## APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91), that is available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

## INQUIRIES

Direct requests for the RFA and inquiries on programmatic issues to:

Dr. Catherine Laughlin  
Chief, Antiviral Research Branch  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3A-22  
6003 Executive Boulevard  
Rockville, MD 20852  
Telephone: (301) 496-8285

Direct inquiries regarding review procedures to:

Dr. Olivia Preble  
Chief, Microbiology and Immunology Review Section  
Scientific Review Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C-20  
6003 Executive Boulevard  
Rockville, MD 20852  
Telephone: (301) 496-8208  
FAX: (301) 402-2638

Direct inquiries regarding fiscal matters to:

Mr. Todd Ball  
Grants Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B-22  
6003 Executive Boulevard  
Rockville, MD 20852  
Telephone: (301) 496-7075  
FAX: (301) 480-3780

#### AUTHORITY AND REGULATIONS

This program is described in the Catalogue of Federal Domestic Assistance No. 93.856, Microbiology and Infectious Diseases Research. Awards are made under the authority of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### WOMEN AND INFANTS TRANSMISSION STUDY (WITS II)

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFA AVAILABLE: AI-92-13

P.T. 34, AA, II; K.W. 0715008, 0715125, 0785055, 0745020

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: October 26, 1992

Application Receipt Date: January 14, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Vaccine Trials and Epidemiology Branch of the Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for funding the continuation of the Women and Infants Transmission Study (WITS). The purpose of this RFA is a competitive renewal of WITS I, a multi-site epidemiologic cohort study of HIV infected pregnant women and their offspring. New sites not participating in WITS I are encouraged to apply, as are current WITS I sites. Specific aims are: (1) to assess the effects of pregnancy on HIV disease progression, (2) determine maternal cofactors related to maternal-infant transmission and timing of transmission, (3) assess early diagnostic techniques to identify HIV-infected fetuses and infants, (4) evaluate the natural history of HIV infection among infants during an era of antiretroviral and other therapeutic modalities, and (5) assess the feasibility of future vaccine trials in this population.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Women and Infants Transmission Study (WITS II), is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-10473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic non-profit and for-profit research institutions; public and private organizations such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

#### MECHANISMS OF SUPPORT

Applicants funded under this RFA will be supported through National Institutes of Health (NIH) Cooperative Agreements (U01). A Cooperative Agreement is a type of assistance through which an award is made to an institution to encourage investigator-initiated research in areas of special importance to the NIH and if substantial programmatic involvement by NIH staff is anticipated. This RFA solicitation represents a onetime

competition for a four year award with a specified deadline for receipt of applications. Program intents for extensions beyond the initial competitive segment are uncertain. If, by the end of the third year of the award, NIAID has not announced an intention to reissue the RFA, awardees who plan to apply for continuing support should contact NIAID program officials for advice on how to recompetete.

#### FUNDS AVAILABLE

Approximately \$5,000,000 will be available for funding the total costs for the initial year of awards made pursuant to this RFA. The NIAID anticipates making four to eight awards as a result of this RFA. The final number of awards to be made is dependent upon receipt of a sufficient number of applications of high scientific merit and availability of funds. The earliest anticipated award date will be July 1993.

#### RESEARCH OBJECTIVES

##### Background

The growing magnitude of the HIV epidemic among women of childbearing age and their infants is becoming apparent in many areas of the United States. The percentages of AIDS cases among women and children are increasing more rapidly than for any other risk groups. In the 1990s, the AIDS epidemic will continue to attack African American and Hispanic women and children in disproportionately high numbers. To date, more than 80 percent of pediatric AIDS cases have been caused by maternal-infant transmission. Moreover, virtually all new cases of pediatric HIV infection in infants and children will be due to maternal-infant transmission.

In the face of this growing epidemic among women and their offspring, there are a number of critical and unanswered questions related to HIV infection during pregnancy and maternal-infant transmission. These include the impact of pregnancy on the health of HIV-infected women, mechanisms and timing of vertical HIV transmission, rates of maternal-infant transmission (overall and among different subpopulations of at-risk pregnant women), as well as understanding cofactors related to HIV transmission.

The Women and Infants Transmission Study II will be a focused continuation of the current Women and Infants Transmission Study (WITS I), which began in 1988. WITS II will continue and expand this prospective natural history cohort study of HIV positive pregnant women and their offspring. It will rely heavily on the core protocols in place for WITS I, but will also encourage new projects that may shed light on our understanding of maternal-infant HIV transmission and early diagnosis of fetal or infant HIV infection. New applicants should mention to the NIAID contact person that they are new applicants, and they will receive a summary of the WITS I protocol, which is necessary in preparing a response to this RFA. Contact Dr. Mary Glenn Fowler, at the address listed under INQUIRIES.

Specific objectives of WITS II are:

- o Determine maternal cofactors related to maternal-infant transmission including assessment of mechanisms and timing of transmission.
- o Determine the impact of pregnancy on the natural history of HIV infection among women through the post partum period including immunologic and virologic changes in pregnant HIV positive women.
- o Evaluate early diagnostic tests to determine infant HIV infection status as rapidly as possible.
- o Determine the natural history of HIV infection among congenitally exposed infants and children in light of antiretroviral, prophylactic, and immune-based therapy.
- o Assess the feasibility of future vaccine trials in a cohort of HIV infected pregnant women by evaluating their attitudes and potential willingness to take part in future clinical vaccine trials for themselves or their infants.

To achieve the objectives of WITS II, the NIAID seeks respondents to help develop and carry out this continuing epidemiologic natural history study of pregnant HIV women and their children. New prospective sites as well as current WITS I sites are encouraged to apply. The template for this study will be the research protocols designed for WITS I. In addition, specific new research studies are also encouraged that may provide critical information directed toward the primary research aims of WITS II.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review. Because this RFA addresses research on the effects of HIV infection among women and their infants, many of whom are from minority race/ethnicity groups, it is anticipated that women and minorities will be adequately represented in applications for this RFA.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by October 26, 1992, a letter of intent that includes a descriptive title of the proposed research and the name, address and telephone number of the Principal Investigator; the identities of other key personnel and participating institutions; and the number and title of the RFA in response to which the application may be submitted. The letter of intent is not binding, does not commit the sender to submit an application, nor is it a requirement for submission of an application.



The letter of intent is to be sent to Dr. Mary Glenn Fowler, at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these cooperative agreements. These forms are available at most institutional offices of sponsored research, the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone 301/496-7441, and from the NIH Program Administrator named above.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA number, RFA AI-92-13 and the title, Women and Infants Transmission Study, must be typed on line 2a of the face page of the application form and the "YES" box must be marked.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, exact, single-sided photocopies, in one package, to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two copies must also be sent directly to:

Dr. Dianne Tingley  
AIDS Scientific Review Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 4C16  
Bethesda, MD 20892

If sending the application by overnight mail or courier service use Rockville, Maryland 20852.

Applications must be received by both DRG and Dr. Tingley by January 14, 1993. Applications received after January 14, 1993 will be returned to the applicant without review.

#### REVIEW CRITERIA

This application must be directed at and address the research objectives identified in this RFA; that portion of the application corresponding to this research plan should follow in form the specific instructions available in the RFA. The primary factors that will be considered in the review of the application will be demonstrated ability or potential to recruit adequate numbers of HIV pregnant women into the study; capability to carry out the clinical and laboratory studies of WITS II including commitment to a multi-site research collaborative effort; and cost efficiency in carrying out the research protocols.

#### AWARD CRITERIA

Awards will be made on the basis of high scientific and technical merit, adequacy of funds, and program relevance. However, after an application have been approved by the National Advisory Allergy and Infectious Diseases Council, NIAID staff reserves the right to give consideration to the following factors in the final selection of applications to be funded: WITS II sites reflect the racial/ethnicity and socioeconomic characteristics of the nation-wide HIV epidemic among women and infants; and reflect the HIV-AIDS incidence/geographic distribution of the epidemic among U.S. women and their infants.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. New applicants should request a copy of the WITS I protocol summary. Direct requests for a copy of the RFA and inquiries concerning programmatic issues to:

Mary Glenn Fowler, M.D., M.P.H.  
Vaccine Trials and Epidemiology Branch  
Division of AIDS  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 2A24  
Bethesda, MD 20892  
Telephone: (301) 496-6177  
FAX: (301) 402-1506 or (301) 480-5703

Direct inquiries concerning fiscal and policy issues to:

Jane Unsworth  
Chief, AIDS Grants Management Section  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 4B25  
Bethesda, MD 20892  
Telephone: (301) 496-7075  
FAX: (301) 480-3780



Direct inquiries concerning the review process and review requirements to:

Dr. Dianne Tingley  
AIDS Scientific Review Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 4C16  
Bethesda, MD 20892  
Telephone: (301) 496-0818  
FAX: (301) 402-2638

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.856 and 93.855. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under Public Health Service Act grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### CLINICAL TRIALS OF CANCER THERAPY WITH BIOLOGICAL RESPONSE MODIFIERS

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFA AVAILABLE: CA-92-28

P.T. 34; K.W. 0755015, 0715035, 0740015

National Cancer Institute

Letter of Intent Receipt Date: October 30, 1992  
Application Receipt Date: December 22, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI) invites applications to establish cooperative agreements for Clinical Trials of Cancer Therapy with Biological Response Modifiers (CATBRMs), for the development of novel approaches to such therapy.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000", a PHS-led national activity for setting priority areas. This RFA, Clinical Trials of Cancer Therapy With Biological Response Modifiers (CATBRMs), is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Groups constituted according to the guidelines given in the RFA (briefly outlined under "RESEARCH OBJECTIVES" below) are eligible to apply. Applying groups may include members from academic, non-profit, and for-profit institutions. Involvement of intramural NIH personnel is limited as described in the RFA. Domestic and foreign organizations and institutions (non-profit or for-profit) are eligible. Governments and their agencies are also eligible. Applications from women and members of minority groups are encouraged.

#### MECHANISM OF SUPPORT

Awards will be made as cooperative agreements (U01). In cooperative agreements, unlike traditional research grants, substantial NCI programmatic involvement with the recipient during performance of the planned activity is anticipated. The nature of NCI staff involvement is described in the RFA. Applicants will be responsible for the planning, direction, and execution of the proposed project. Specifically, the CATBRM study group is responsive to the requirements and conditions set forth in the RFA. The Principal Investigator defines the details for the project in accordance with the Terms of Cooperation, retains primary responsibility for the performance of the activity, and agrees to accept close coordination, cooperation, and assistance of NCI extramural staff (through the NCI Program Director) in all aspects of scientific and technical management of the project. However, there is no intent, real or implied, for NCI staff to direct CATBRM activities or to limit the freedom of investigators.

This RFA is a reissuance of RFA CA-92-01. Applicants who did not apply to the first announcement, or who applied but did not receive an award, are encouraged to respond to this RFA. However, this reissued RFA is a one-time solicitation. Generally, future unsolicited competing renewal applications will compete as research project applications with all other investigator-initiated applications. If the NCI determines that there is sufficient continuing program need, the NCI will invite recipients of awards under this RFA to submit competitive continuation cooperative agreement applications for review.

## FUNDS AVAILABLE

NCI plans to make up to six awards for project periods up to four years, and has set aside \$1.5 million total costs for the initial year's funding. The total funding level and number of awards to be made is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Cancer Institute, awards pursuant to this RFA are contingent upon continuing availability of funds.

Applicants may request no more than four years of support. The earliest possible starting date for the initial annual period will be July 1, 1993.

## RESEARCH OBJECTIVES

Cooperative Agreements will be established to support Clinical Study Groups for Cancer Therapy with Biological Response Modifiers (CATBRMs), for the design and execution of novel clinical trials with biological response modifiers (BRMs). CATBRM groups will be peer-reviewed groups of highly experienced clinical and preclinical investigators who have the unique technical capabilities to study new agents in early clinical trials and to address hypothesis-driven issues of mechanisms of action. The "Research Goals and Scope" of the RFA will require a novel plan for clinical study of a given new agent or agents, adequately supported by prior preclinical, and if available, clinical, results. The application must describe how its objectives are in accord with the applicant's own interests and experience. The applicant must provide evidence of access to the agent(s) proposed for study. A detailed protocol for an initial clinical trial must also be included. The NCI will facilitate the institution of a peer-reviewed, investigator-initiated trial, participating according to Terms of Cooperation outlined in the RFA.

Each CATBRM study group will be composed of: a Principal Investigator; one or more laboratory programs, each headed by a Program Leader, with the demonstrated expertise to design and carry out assays for the appropriate monitoring of patients on the study; one or more clinical programs, each headed by a Program Leader, with demonstrated expertise in conducting clinical trials of BRMs; and the NCI Program Director.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by October 30, 1992, a short letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of this RFA.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows ICD staff to estimate the potential review workload and to avoid conflict of interest in the review.

Letters of intent are to be sent to:

Jon T. Holmlund, M.D.  
Biological Resources Branch  
Biological Response Modifiers Program  
National Cancer Institute  
NCI-FCRDC, Building 1052, Room 253  
Frederick, MD 21702-1201  
Telephone: (301) 846-1098  
FAX: (301) 846-5429

## APPLICATION PROCEDURES

The deadline for receipt of applications is December 22, 1992. Applications received after this date will be returned without review to the applicant.

The regular research grant application form PHS 398 (rev. 9/91) is to be used in applying. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7741; and from the NIH Program Administrator named below. The RFA label available in the application form PHS 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources are requested to identify the GCRC as a resource for conducting the proposed research.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the DRG for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If an application is not responsive to the RFA, it will be returned to the applicant and the proposed Principal Investigator will be contacted to determine whether submission for review in competition with unsolicited applications (e.g., as an

R01 or P01, after appropriate modification) at the next review cycle is desirable to the applicant. Questions concerning the relevance of proposed research to the RFA may be directed to the NIH Program Administrator listed under INQUIRIES.

In cases where the number of applications is large compared to the number of awards to be made, the NCI may conduct a preliminary scientific peer review to eliminate those which are clearly not competitive for award. The NCI will remove from further competition those applications judged to be noncompetitive and notify the Principal Investigator and institution official.

Those applications judged to be both competitive and responsive will be further evaluated, using review criteria described in the RFA, for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. Following peer review, the applications will receive a second-level review by the National Cancer Advisory Board, which considers the special needs of the Institute and the priorities of the National Cancer Program.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Jon Holmlund, M.D.  
Program Director, Biological Resources Branch  
Biological Response Modifiers Program  
National Cancer Institute-FCRDC  
Building 1052, Room 253  
Frederick, MD 21701-1201  
Telephone: (301) 846-1098  
FAX: (301) 846-5429

Direct inquiries regarding fiscal matters to:

Ms. Katharine Schulze  
Grants Management Specialist  
Grants Administration Branch  
Executive Plaza South, Room 242  
6120 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-7800, Ext. 16  
FAX: (301) 496-8601

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.395, (Cancer Treatment Research). Awards are made under authorization of the Public Health Service Act, Title, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SPECIALIZED RESEARCH CENTER PROGRAMS AND CENTER CORE GRANTS TO SUPPORT RESEARCH IN REPRODUCTION

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFA AVAILABLE: HD-94-01

P.T. 04; K.W. 0413002, 0710110, 0710115, 0710030

National Institute of Child Health and Human Development

Letter of Intent Receipt Date: January 2, 1993

Application Receipt Date: May 18, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Reproductive Sciences Branch (RSB), Center for Population Research (CPR), National Institute of Child Health and Human Development (NICHD), supports research on reproduction which relies on a variety of approaches in biomedical sciences. Among the grant mechanisms used to provide research support, the RSB uses:

(1) Specialized Research Centers (P50s) which are integrated groups of research projects and supporting core service facilities. The research activities included in such project grants must comprise, by definition, a multidisciplinary approach to biomedical problems in reproduction. Although these research programs may have more than one theme, focus, or emphasis, all of the projects must be responsive to one or more of the specific areas of reproductive research which constitute the mission of the RSB, CPR, NICHD.

(2) Center Core Grants (P30s) that support Center Core facilities designed to enhance a group of existing federally supported research projects within the purview of the RSB, CPR, NICHD. Such Center awards require



a critical mass of individual, reproductive-oriented awards whose productivity and quality would be increased by support from central technical facilities.

Institute policy requires recompetition for the P30/P50 Center Program in the Reproductive Sciences Branch.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Specialized Research Center Programs and Center Core Grants to Support Research in Reproduction, is related to the priority area of family planning. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private. Foreign organizations are not eligible. New Specialized Research Center Grant (P50) applications may not request more than \$600,000 in direct costs for the first year. New Center Core Grant (P30) applications may not request more than \$500,000 in direct costs for the first year. Renewal applications from existing P30 or P50 centers may not request initial year direct costs exceeding 120 percent of the Council recommended direct costs for the final year of the preceding project period. Unless prior written approval of the NICHD has been obtained, applications with requests exceeding these guidelines will be administratively withdrawn by the NICHD and returned to the applicant. Applications prepared for this competition may not propose multi-institutional consortiums.

#### MECHANISM OF SUPPORT

This RFA will use the Specialized Research Center Program (P50) and Center Core (P30) Grant mechanism to support research in reproduction. The total project period for applications submitted in response to this RFA is five years. The anticipated award date will be April 1, 1994.

#### FUNDS AVAILABLE

Although this solicitation is included in the fiscal plans for FY 1994, support for these center grants is contingent upon the receipt of funds for these purposes by the NICHD. The number of grants to be awarded is also contingent upon a sufficient number of applications receiving a high enough level of merit to be considered for an award. It is expected that up to four awards will be made as a result of this announcement within the expected total cost limit of \$3,600,000 available for the first year. At present, the RSB supports a fixed number of centers with a commitment of five years of support that is competitively renewable for additional five-year periods. Support for one P50 Center and three P30 Centers ends in FY 1994 and it is anticipated that these Centers will submit renewal applications. Although there are no additional Center awards available at this time, new groups of investigators are invited to compete with the current awardees for the existing four awards.

#### RESEARCH OBJECTIVES

The ultimate goals of biomedical research in the reproductive sciences are to develop new knowledge leading to clinical applications that will enable men and women to control their fertility with methods that are safe, effective, inexpensive, reversible, and acceptable to various population groups, and to overcome problems of infertility and reproductive disorders. Domestic U.S. Reproductive Sciences centers designated as "Specialized Reproductive Sciences Research Center" (P50s) and as "Reproductive Sciences Research Centers" (P30s) are awarded for the support of comprehensive reproductive research programs of high quality that focus on topics deemed to be of high priority and significance because of their critically important relationship to the mission of the RSB, CPR.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

It is strongly recommended, but not mandatory, that potential applicants send a letter of intent to the RSB staff at the address listed below by January 2, 1993. This letter is to include a list of the titles of the relevant research projects to be associated with the proposed center and provide the names of the relevant key investigators. The letter of intent is to be received by the RSB no later than January 2, 1993, but applicants are encouraged to send it as soon as they decide to apply for the grant so that the RSB staff can be of maximum assistance in the application process. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NICHD staff to estimate the potential review workload and avoid conflict of interest in the review. The letter of intent is to be sent to the RSB staff contact listed under INQUIRIES.

#### APPLICATION PROCEDURES

Center grant applications must be structured in accordance with the specific policy and formatting guidelines presented in the RFA and the instructions found in the publications entitled either "P50 Specialized Research



Center Grant Guidelines" or "P30 Center Core Grant Guidelines" that are available from the NICHD office listed below. Such guidelines require, for example, certain tabulations in addition to the usual instructions for the grant application form PHS 398 (rev. 09/91) used to prepare these applications. The current policies and requirements that govern the research grant programs of NIH will prevail (Code of Federal Regulations, Title 42, Part 52 and Title 45, Part 75).

#### REVIEW CONSIDERATIONS

An administrative review of the application will be performed by NIH staff for conformance to NIH policy and NICHD guidelines, as well as for relevance to the program purview of the RSB. Applications that fail to comply with NIH policy and/or NICHD guidelines will be formally returned to the applicant. Applications will be evaluated by the Population Research Committee, NICHD in November 1993. The second level review will be made by the National Advisory Child Health and Human Development Council in January 1994. Review procedures and criteria are detailed in the P50 SPECIALIZED RESEARCH CENTER GRANT GUIDELINES and P30 CENTER CORE GRANT GUIDELINES (available from NICHD offices listed below).

#### AWARD CONSIDERATIONS

The earliest possible funding date is April 1, 1994. Funding decisions will be based on the IRG review and NACHHD Council recommendations, program relevance, and the availability of funds.

#### INQUIRIES

For further information and a copy of the RFA, contact:

Julia Lobotsky, M.S.  
Reproductive Sciences Branch  
Center for Population Research  
National Institute of Child Health and Human Development  
Building 6100, Room 8B01  
Bethesda, MD 20892  
Telephone: (301) 496-6515

To obtain copies of the NICHD Policy and Formatting Guidelines for P30 and P50 center grant applications, contact:

Laurance Johnston, Ph.D.  
Division of Scientific Review  
National Institute of Child Health and Human Development  
Building 6100, Room 5E01  
Bethesda, MD 20892  
Telephone: (301) 496-1696

For information on budget and fiscal matters, contact:

Melinda Nelson  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Building 6100  
Bethesda, MD 20892  
Telephone: (301) 496-5481

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.864, Population Research. Awards will be made under the authority of the Public Health Service Act 301 (42 USC 241) and 441 (USC 289d) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 or Health Systems Agency review.

#### CELL AND MOLECULAR BIOLOGY OF MEGAKARYOCYTOPOIESIS

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFA AVAILABLE: HL-93-03-B

P.T. 34; K.W. 0780015, 0780020, 0760003, 0760020, 1002008, 1002019

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: January 15, 1993

Application Receipt Date: March 15, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

#### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) announces the availability of an RFA on the above subject. The purpose of this initiative is to encourage research that may contribute to better understanding of regulation of the proliferation and maturation of megakaryocytes and the control of platelet production. It

is hoped that the information generated will allow manipulation of megakaryocytopoiesis and platelet levels in pathological conditions.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Cell and Molecular Biology of Megakaryocytopoiesis, is related to the priority areas of platelet disorders and bone marrow transplantation. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-782-3238).

#### ELIGIBILITY REQUIREMENTS

All domestic and foreign, public and private, for-profit and non-profit institutions and organizations are eligible to apply in response to this RFA. Awards in connection with this announcement will be made to foreign institutions only for research of very unusual merit, need and promise, and in accordance with PHS policy governing such awards. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29).

#### MECHANISM OF SUPPORT

This RFA solicits applications for the National Institutes of Health (NIH) individual research grant (R01) and FIRST (R29) awards and is a one-time solicitation. Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project. Up to five years of support may be requested. At the end of the official award period, renewal applications may be submitted for peer review and competition for support through the regular grant program of the NHLBI. It is anticipated that support for the present program will begin in September 1993. Administrative adjustments in project period and/or amount of support may be required at the time of the award. All current policies and requirements that govern the research grant programs of the NIH will apply to grants awarded in connection with this RFA.

#### FUNDS AVAILABLE

Although the financial plans for fiscal year 1993 include \$1.5 million for this program, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that about six grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and on the availability of funds. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded. If collaborative arrangements involve sub-contracts with other institutions, the NHLBI Grants Operations Branch (telephone 301-496-7257) may be consulted regarding procedures to be followed.

#### RESEARCH OBJECTIVES

The following are only examples and prospective applicants are urged to use their own ideas as to the area of research.

##### Development of Cell Lines and Culture Systems

The critical molecular events that lead to commitment of progenitor cells to the megakaryocytic lineage and to complete maturation of megakaryocytes to platelet production have not been identified. These studies require the development of cell lines that can enter and complete the normal maturation cycle. Immortalized cell lines could be generated that can be triggered to undergo differentiation under restricted conditions. Another approach would be to develop bone marrow culture systems that allow the transition of stem cells to megakaryocytes to be specifically monitored. This approach could employ precursor cells isolated from transgenic mice that possess megakaryocyte-specific promoters coupled to reporter molecules in conjunction with purified hematopoietic growth factors. The role of known oncogenes, growth factor receptors, and other signaling proteins could be investigated in the above systems with dominant negative suppressor techniques, antisense approaches, or injection of specific neutralizing antibodies. The function of previously unidentified components might be sought by somatic cell genetic techniques coupled to expression cloning methods.

##### Nuclear and Cytoplasmic Development

The biochemical steps that are responsible for the development and extent of polyploidy and for maturation of the cytoplasm and the formation of granule and membrane systems are not defined. The molecules that are specific to megakaryocytes and to different stages of development must be defined; new markers other than those currently used in studies of platelets should be sought. The cis acting regions and transacting factors of genes specifically expressed in megakaryocytes should be determined, and the effects of hematopoietic growth factors and cytokines on these events should be assessed.

Specific areas of study that might elucidate nuclear development include the role of cyclins, kinases, phosphatases, and contractile proteins in endomitosis. Specific areas of study regarding cytoplasmic development include stage-specific events in granule formation and synthesis of membrane and cytoskeletal components, including targeting of proteins to specific structures. The mechanism by which the cytoplasm becomes organized into the mature platelets is unknown, and studies that could address this question would be useful. It would also be important to identify the specific growth factors that control nuclear and cytoplasmic development and platelet formation.

## Sensors and Signals

Investigations are needed to clarify the sensors and molecular signals that modulate the plasma levels of the megakaryocyte specific growth factors and thereby regulate megakaryocytopoiesis.

## Platelet Production

Newly available techniques might be used to clarify questions related to platelet production. For example, megakaryocytes that have been genetically labeled with short-lived reporter molecules might serve as *in vivo* markers for quantitating platelet production. The site of megakaryocyte fragmentation might be determined by injecting the labeled cells and measuring the formation of the circulating platelets.

## Genetic Defects in Megakaryocytopoiesis

Chromosomal abnormalities have been associated with megakaryocytic leukemias, notably in Down syndrome and in adult leukemias in otherwise genetically normal individuals. Other congenital syndromes that include defects in megakaryocytopoiesis have been identified, such as TAR syndrome and Epstein's syndrome. In addition, a number of animal models of defective megakaryocytopoiesis have been described. Characterization of the genetic abnormalities in these various conditions could provide useful information on the factors regulating megakaryocytopoiesis.

## Special Requirements

The NHLBI will sponsor annual meetings to encourage the exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants must request additional travel funds for one meeting each year to be held in Bethesda, MD. Applicants must also include a statement in the applications indicating their willingness to participate in such meetings.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

The NHLBI requests that prospective applicants submit a letter of intent that includes a descriptive title of the proposed research and identification of other participating institutions. Such letters are requested only for the purpose of providing an indication of the number and scope of applications to be received; therefore their receipt is not acknowledged. A letter of intent is not binding, will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter of intent, which must be received by January 15, 1993, is to be sent to:

Dr. Charles L. Turbyfill  
Division of Extramural Affairs,  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 553  
Bethesda, MD 20892

## APPLICATION PROCEDURES

Applications are to be submitted on the research grant application form PHS 398 (rev. 9/91). This form is available from most applicant institution's office of sponsored research or business office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Ave, Room 449, Bethesda, MD 20892. FIRST Award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Application Receipt Date: March 15, 1993

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by the DRG and for responsiveness to the objectives of the RFA by the NHLBI. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NHLBI staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications judged to be responsive will be reviewed for scientific and technical merit by an initial review group that will be convened by the Division of Extramural Affairs, NHLBI, solely to review these applications.

This initial review will include a preliminary evaluation to determine scientific merit relative to the other applications received in response to the RFA (triage); the NHLBI will withdraw from further consideration applications judged to be noncompetitive and notify the Principal Investigator/program director and the applicant organization. Those applications judged to be competitive will be further evaluated for scientific/technical merit by the usual peer review procedures.

The second level review will be by the National Heart, Lung, and Blood Advisory Council.



## INQUIRIES

Inquiries regarding this program and requests for the RFA document to:

Dr. Pankaj Ganguly  
Chief, Thrombosis and Hemostasis Branch  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Federal Building, Room 5C14  
Bethesda, MD 20892  
Telephone: (301) 402-2237  
FAX: (301) 496-9940

Fiscal and administrative matters to:

Ms. Jane R. Davis  
Chief, Blood Division Grants Management Section  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A15  
Bethesda, MD 20892  
Telephone: (301) 496-7257  
FAX: (301) 402-1200

## AUTHORITY AND REGULATIONS

The programs of the Division of Blood Diseases and Resources, NHLBI, are described in the Catalog of Federal Domestic Assistance No. 93.839. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal Regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or to Health Systems Agency review.

## ONGOING PROGRAM ANNOUNCEMENTS

### SELECTIVE COGNITIVE DEFICITS IN NEURODEVELOPMENTAL DISORDERS

NIH GUIDE, Volume 21, Number 36, October 9, 1992

PA: PA-93-004

P.T. 34; K.W. 0414005, 0715138, 1002030

National Institute of Neurological Disorders and Stroke

### PURPOSE

The National Institute of Neurological Disorders and Stroke (NINDS) encourages the submission of research grant applications to pursue a promising new approach to cognitive neuroscience that will identify relations between cognitive function and neurostructure through the study of specific, atypical patterns of cognitive deficit associated with neurodevelopmental syndromes of known or suspected biological origin. Examples of three clinical entities that can be studied from this perspective are Williams syndrome, Turner syndrome and autism. An FY 91 NINDS workshop was devoted to the discussion and confirmation of the usefulness of in depth, systematic investigation of patterns or profiles of selective cognitive impairment in these unusual conditions.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention goals of "Healthy People 2000," a PHS-led national activity for setting priorities. This Program Announcement, Selective Cognitive Deficits in Neurodevelopmental Disorders, is related to the priority areas of infant health, chronic disabling conditions, and the related area of the neurological basis of cognition. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: No. 017-001-474-0, or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29), program project grants (P01), and center grants (P50). Applications from minority individuals and women are encouraged.

### MECHANISMS OF SUPPORT

The support mechanisms for grants in this area will be the traditional investigator-initiated research project grant (R01), the FIRST award (R29), the program project grant (P01), and the center grant (P50). As consistent with the aforementioned mechanisms, the Principal Investigator or program director, as well as any participating investigators, will plan, direct, and perform the research. Applicants for program project grants should contact the NINDS representative listed below as early as possible in the planning stages.



## RESEARCH OBJECTIVES

Most of the knowledge about the neurological bases of cognitive function in humans has been learned from studies of central nervous system trauma or disease in adults. Certain experiments of nature seen in neurodevelopmental syndromes affect the central nervous system in unique ways by producing specific as opposed to generalized cognitive deficit. Studies of these disorders, utilizing neurobiological and behavioral techniques, can be expected to yield new insights into the localization of cognitive function and the developmental course of the syndromic cognitive profiles.

An example of this approach is an ongoing study of the biological basis of language and other cognitive functions in which behavioral, neuroanatomic, and neurophysiologic studies are being carried out in patients with Williams syndrome, a rare metabolic disorder. Children with this sporadically occurring condition have distinctive facial characteristics, low birth weight, digestive disorders in infancy, mental retardation, mild microcephaly, apparent sensitive hearing and supravalvular aortic stenosis. A unique behavioral profile has been identified in these patients in which there is a striking fractionation of higher cortical functions with linguistic abilities selectively preserved in the face of severe cognitive deficits. Studies of the development of language in Williams syndrome children are being conducted in conjunction with studies of brain structure and function to address specific questions about the neural substrate for this unusual neuropsychological profile. This research, and similar investigations, will contribute to our understanding of brain organization for language, and other cognitive functions, using a specific neurodevelopmental disorder as a model. Such an approach provides an unusual opportunity to investigate central issues of developmental cognitive neuroscience.

In a parallel and possibly related investigation of autism, a developmental disorder characterized by a profound deficiency in social knowledge, affect, and communication, a new finding demonstrates severe impairment in ability to shift attention, a necessary developmental precursor to social communication. Evidence is presented that relates this deficit to neuroanatomic abnormalities found in the cerebellum of autistic patients in both autopsy and magnetic resonance imaging (MRI) studies and to findings of damage to the parietal lobe of the cerebrum as well. There is a clear contrast between autism and Williams syndrome in both behavioral deficits and neuroanatomic findings. Most autistic children have aberrant language development and marked deficits in social communication and patients with Williams syndrome have spared linguistic abilities, but general cognitive impairment, and show an intensity of affect, especially in social interaction. The basis for these behavioral distinctions may be the differences in neocerebellar structures for which the autistic and Williams syndrome subjects show divergent morphology.

Turner syndrome is a genetic disorder associated with monosomy X that is characterized by a variety of somatic and cognitive deficiencies. The classical features of the syndrome include short stature, webbed neck, a broad chest, cubitus valgus, and failure of gonadal development. While females with Turner syndrome typically have normal verbal IQ scores, they consistently show selective impairments in tasks that are included in tests of performance IQ. The results of most studies present clear impairment in performance in spatial rotation and left-right discrimination tasks. Other studies report deficits in visual-spatial memory, visual-motor coordination, and motor learning. Slower motor responses have also been demonstrated in females with Turner syndrome. The etiology of these cognitive deficits is still unknown and there is considerable inter-individual variation in the neurocognitive phenotype of Turner syndrome. However, right hemisphere involvement is certainly indicated. Current studies are addressing the problems of variations in patterns of cognitive abilities with variations in karyotype in Turner syndrome, changes in patterns of cognitive abilities in response to hormone therapies, sources of deficits in social cognition, and neurophysiological indications (event-related potentials) of altered brain development in Turner syndrome.

More extensive investigations of the etiologies and effects of these syndromes and carefully designed studies of other syndromes and conditions that result in atypical patterns of cognitive deficit are encouraged. Examples are various types of hydrocephaly and the fragile X syndrome. Because of the multi-leveled approach--behavioral, neurophysiological, and neuroanatomic--and the likelihood of small samples, multidisciplinary and collaborative studies will be most appropriate.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Section 1-4 of the research plan AND summarized in Section 5, Human Subjects. Applicants/offers are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants. For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed and the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) according to instructions contained in the application kit. Application kits are available from most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

Check "yes" in item 2a on the face sheet of the application and type "Selective Cognitive Deficits in Neurodevelopmental Disorders." FIRST Award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review. Applicants for the P01 or P50 must use the application format described in the NINDS pamphlet, NINDS GUIDELINES: PROGRAM PROJECT AND RESEARCH CENTER GRANTS (Revised June 1992). Deadlines for the receipt of applications are February 1, June 1, and October 1. The completed original application and five exact copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

If the application is for a program project or center grant, please send the original and three copies to the Division of Research Grants. An additional two copies sent to the address below would be useful for expediting the processing of applications for multidisciplinary efforts.

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications will be judged on scientific merit and program relevance in accordance with NIH policy and procedures involving peer review. An initial review will be made by an appropriate study section of the Division of Research Grants for research grants (R01) and FIRST awards (R29), and by an appropriate institute committee for program projects (P01) and centers (P50). A second level of review will be made by an appropriate national advisory council.

#### AWARD CRITERIA

Applications assigned to the NINDS will compete for available funds with all other approved applications assigned to the NINDS. The following will be used in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

For further information regarding this announcement, potential applicants may write or call:

Sarah H. Broman, Ph.D.  
Developmental Neurology Branch  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 8C-06  
Bethesda, MD 20892  
Telephone: (301) 496-5821

For fiscal and administrative inquiries regarding this announcement, potential applicants may write or call:

Dwight Mowery  
Grants Management Branch  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
Bethesda, MD 20892  
Telephone: (301) 496-9231

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.853 and 93.854. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-150, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ARTHRITIS & SKIN DISEASES (MINORITY POPULATIONS)

NIH GUIDE, Volume 21, Number 36, October 9, 1992

PA NUMBER: PA-93-005

P.T. 34, FF; K.W. 0715010, 0715185

National Institute of Arthritis and Musculoskeletal and Skin Diseases

### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases invites investigator-initiated grant applications and supplemental applications to carry out clinical and epidemiologic studies on the etiology, treatment, and prevention of arthritis, musculoskeletal, and skin diseases in minority populations and other populations at special risk.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Arthritis and Skin Diseases (Minority Populations), is related to the priority area of chronic disabling conditions and surveillance objectives. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Research grant applications may be submitted by domestic and foreign for profit and non-profit organizations, public and private, such as local governments, and eligible agencies of the Federal Government. Applications with minority individuals and women as Principal Investigators are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29). Applicants for the Clinical Investigator Awards (K08) and Individual National Research Service Awards (F32) must be U.S. citizens, non-citizen nationals, or non-citizens lawfully admitted for permanent residence. Applicants for the F32 Award must have received a doctorate degree as of the beginning date of the NRSA appointment. Applicants for the K08 Award must have an M.D. or equivalent degree. Applicants for the Fogarty International Research Collaboration Award (FIRCA) Award must be U.S. scientists who are Principal Investigators of NIH Research Project Grants (R, P, or U01 series) that are active and funded during the proposed FIRCA grant award period. Recipients of K awards are not eligible. For the FIRCA Award, the foreign collaborator's institution must be located in a country in the geographical regions commonly known as Central and Eastern Europe (including the former USSR), Latin America, and the non-US Caribbean.

### MECHANISMS OF SUPPORT

Applications for the following mechanisms are considered appropriate responses to this announcement: the traditional research project grant (R01) and the FIRST Award (R29), the Clinical Investigator Award (K08), and the Individual National Research Service Award (F32). In addition, the FIRCA funding mechanism may be used by NIH grantees in the U.S. to collaborate with foreign investigators. Joint efforts between U.S. and foreign investigators are encouraged.

Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also.

### SUMMARY

#### o Background

Major gaps in knowledge still exist about the incidence, prevalence, and natural history of most of the rheumatic, musculoskeletal, and skin diseases. The skin diseases in particular have lacked epidemiologic research. Although both cross-sectional and longitudinal studies are lacking for many diseases, the greatest need is for longitudinal investigations. Some population-based longitudinal data sources are available for studies of rheumatic diseases and osteoporosis, e.g., Framingham, Massachusetts; Rochester, Minnesota; NHANES I and Followup; and the Study of Osteoporotic Fractures (SOF).

In the past decade, epidemiologic studies have made some progress in describing the frequency of osteoarthritis and some skin diseases, based upon nationally collected data by the National Center for Health Statistics. Epidemiologic studies from defined populations have contributed knowledge about cohorts at increased risk of disease, e.g., rheumatoid arthritis in Pima Indians and the higher incidence, prevalence, and mortality of systemic lupus erythematosus in Black females than in Caucasian and male populations. However, the key question, why some cohorts remain at increased risk of disease, is still unanswered.



In general, less is known about the occurrence of arthritis, musculoskeletal, and skin diseases in American Blacks than in whites. Even less is known about other American minority groups. Data are also lacking on these diseases in children and the elderly.

#### o Research Objectives and Scope

The primary objective of this program announcement is to foster epidemiologic research in minority groups and other populations at special disease risk. Studies to be encouraged include:

- o The descriptive pattern of arthritis, musculoskeletal and skin diseases in populations
- o The etiology and modes of transmission of these diseases, including the relative contribution of both genetic and environmental factors influencing both the onset and course of the disease
- o Studies of disease burden, specifically on the frequency, cost, and personal and social sequelae of arthritis and musculoskeletal and skin diseases
- o New diagnostic technologies to update or develop criteria for the diagnosis and staging of many rheumatic and skin diseases and to define homogeneous clinical subsets for epidemiologic and basic science studies
- o Studies to generate and test etiologic hypotheses, especially for less studied rheumatic, musculoskeletal, and skin diseases
- o Family studies to evaluate the interplay of genetic and environmental contributions to the development and progression of rheumatic, musculoskeletal, and skin diseases
- o Longitudinal studies to describe the prognosis and outcomes among patients with rheumatic, musculoskeletal, and skin diseases, and to identify risk factors for disease onset, progression, and disability
- o Practical outcome assessment tools to define the impact of different medical, surgical, and rehabilitation management approaches for arthritis, musculoskeletal and skin diseases

#### STUDY POPULATIONS

Epidemiologic studies of the general population at risk for disease, as well as patient populations that have been diagnosed to have the diseases, will be accepted. Although new research projects are desired, applications based on on-going studies that were conceived for reasons other than the purposes of this program announcement are also encouraged.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.



All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications for the R01, R29, K08, and FIRCA awards are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. FIRST (R29) Award applications must include at least three sealed letters of reference attached to the face page of the original application. First Award applications submitted without the required number of reference letters will be considered incomplete and will be returned to the applicant without review. The receipt dates for applications for AIDS-related research are also found in the PHS 398 (rev. 9/91) application kit. Supplemental application instructions for the K08 Award and the application dates are available in the publication "The K Awards" (rev. 10/91). Supplemental application instructions for the FIRCA award are available from the John E. Fogarty International Center. Applications for the FIRCA Award must include a letter of collaboration from the foreign investigator and the foreign investigator's biographical sketch, resources, and environment. Applications for the F32 Award are to be submitted on form PHS 416-1 and must include letters of reference and other supplemental material.

Application kits and information booklets including relevant receipt dates are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

The completed original application and the appropriate number of legible copies, as specified in the application kits, must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications will be reviewed for scientific and technical merit in accordance with the standard NIH peer review procedures. FIRCA Award applications will be reviewed by an initial review committee convened by the Fogarty International Center.

Following scientific-technical review, the applications will receive a second-level review by an appropriate advisory council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

Additional criteria for R29 and F32 applications include the potential for the applicant to carry out independent research, the quality of education, scientific training, research experience, and commitment to a research career, as well as the institutional commitment. Further criteria for F32 applications include the quality of the sponsor and training environment and the reference reports.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Ms. Reva C. Lawrence  
Epidemiology/Data Systems Program Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Building 31, Room 4C-13  
Bethesda, MD 20892  
Telephone: (301) 496-0434

Direct inquiries regarding fiscal matters to:

Ms. Diane M. Watson  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 4A15C  
Bethesda, MD 20892  
Telephone: (301) 496-7257

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

ERRATUM



DIETARY PATTERNS AND BLOOD PRESSURE

NIH GUIDE, Volume 21, Number 36, October 9, 1992

RFA: HL-92-11-P

P.T. 34; K.W. 0710095, 0715115, 0755015

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: December 1, 1992

Application Receipt Date: January 15, 1993

This is to announce a change in the Letter of Intent Receipt Date and the Application Receipt Date that published in the NIH Guide for Grants and Contracts, Vol. 21, No. 34, September 25, 1992.

The new Letter of Intent Receipt Date is December 1, 1992 (changed from November 1, 1992).

The new Application Receipt Date is January 15, 1993 (changed from December 1, 1992).

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 37  
October 16, 1992

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

# NOTICES

## ADAMHA/NIH REORGANIZATION

NIH GUIDE, Volume 21, Number 37, October 16, 1992

P.T. 34; K.W. 1014006

National Institutes of Health  
Alcohol Drug Abuse and Mental Health Administration

On July 10, 1992, President Bush signed into law the ADAMHA Reorganization Act of 1992 (P.L. 102-321) merging the three research institutes of the Alcohol Drug Abuse and Mental Health Administration (ADAMHA) with the National Institutes of Health (NIH) and establishing a new agency, the Substance Abuse and Mental Health Services Administration. On October 1, 1992, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH) merged with the NIH.

The NIAAA, NIDA, and NIMH will continue to accept research grant and research training applications as they have in the past. No substantial changes in policy or procedure are anticipated. If changes or adjustments of policy or procedure are necessary, it will be announced in the NIH Guide. The ongoing policy previously announced jointly by the NIH/ADAMHA on the inclusion of women and minorities in clinical research study populations, will continue in force until revised or reissued.



CORE IMMUNOLOGY LABORATORY FOR ASSESSMENT OF AIDS VACCINES IN PRIMATES

NIH GUIDE, Volume 21, Number 37, October 16, 1992

RFP: NIH-NIAID-DAIDS-93-15

P.T. 34; K.W. 0715008, 0740075, 0710070, 0755010

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) has a requirement to provide for the centralized performance of immunological assays to support preclinical AIDS vaccine trials in primates. The purpose of this contract is to support the NIAID in its mission to stimulate research towards discovery and testing of prototype vaccines for the acquired immunodeficiency syndrome (AIDS). The NIAID requires a Primate Core Immunology Laboratory to assay specimens from macaques, chimpanzees, or other primates for humoral and cellular immune responses induced by immunization with prototype Simian Immunodeficiency Virus (SIV) and Human Immunodeficiency Virus (HIV) vaccines. This effort will support the research of AIDS investigators, including three SIV Vaccine Evaluation Units (SIV VEU), a Chimpanzee Unit, the National Cooperative Vaccine Evaluation Group (NCVVG), the AIDS Vaccine Evaluation Group (AVEG), and other programs initiated by NIAID. Specifically, the selected contractor will be responsible for: (1) performing specific evaluations of cellular immune responses induced by vaccination; (2) performing specific evaluations of humoral immune responses induced by vaccination; (3) adapting, standardizing, providing quality assurance, and performing any newly developed immunological assays that may be identified during the period of the contract as offering potential for assessment of vaccine safety and immunogenicity; (4) receiving, cataloging, tracking, and maintaining an inventory of the specimens arriving for evaluation; and (5) maintaining test result database and transferring data to the AIDS Vaccine Clinical Trials Network (AVCTN) Data Coordinating and Analysis Center (DCAC). This is an announcement for an anticipated Request for Proposals (RFP). The issuance of RFP NIH-NIAID-DAIDS-93-15 will be on or about October 16, 1992, and proposals will be due by the close-of-business on January 5, 1993. It is anticipated that one contract will be awarded as a result of this solicitation and that the contract will have a five-year period of performance. A completion type cost-reimbursement contract is anticipated. Requests for the RFP must be directed in writing to:

Kristi Hofacker, Contract Specialist  
Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C07  
6003 Executive Boulevard  
Bethesda, MD 20892

Provide this office with three self-addressed mailing labels. Telephone inquiries will not be honored and all inquiries must be in writing. A short-form version of the RFP will be provided first. That version includes only the Statement of Work and the Evaluation Criteria to be used for selection of the awardee. After examining this document, a full-text version of the RFP must be requested, in writing, for those offerors interested in responding. FAX requests are acceptable for full-text versions of the RFP only (FAX: 301-402-0972). All proposals from responsible sources will be considered by the NIAID. This advertisement does not commit the Government to award a contract.

NIDCD-NASA CENTER FOR VESTIBULAR RESEARCH

NIH GUIDE, Volume 21, Number 37, October 16, 1992

RFA AVAILABLE: DC-93-003

P.T. 34; K.W. 0785005, 1002061

National Institute on Deafness and Other Communication Disorders

Letter of Intent Receipt Date: November 15, 1992  
Application Receipt Date: December 22, 1992

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

PURPOSE

The National Institute on Deafness and Other Communication Disorders (NIDCD) of the National Institutes of Health (NIH), in collaboration with the Life Sciences Division of the Office of Space Science and Applications, National Aeronautics and Space Administration (NASA), invite applications for the support of a ground-based research center to carry out research applicable to vestibular issues associated with space flight and fundamental knowledge about the vestibular system. In addition to research, the Center will include a research training component. The Center will conduct a number of research projects in humans and/or animals integrated into a program and centered around the vestibular control of balance and posture and the regulation of locomotion and other volitional movements.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, NIDCD-NASA Center

for Vestibular Research, is related to the priority areas of physical activity fitness, educational and community-based programs, unintentional injuries, occupational safety and health, diabetes and chronic disabling diseases, and clinical prevention services. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

#### MECHANISMS OF SUPPORT

This RFA will use the NIH Comprehensive Center (P60) grant mechanism. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant.

The total project period for applications submitted in response to the present RFA must be five years. The anticipated award date will be July 1, 1993.

This RFA is a one-time solicitation. At present, the NIDCD and NASA have made no commitment to continue support for the Center beyond five years.

#### FUNDS AVAILABLE

One Center will be supported jointly by NIDCD and NASA at a level of up to \$1 million total (direct plus indirect) costs per annum for a project period of five years. Although this Center is provided for in the financial plans of the NIDCD and NASA, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The major research objective of this RFA is to characterize the relative roles of the semicircular canal, otolithic organ and canal-otolithic organ interactive inputs to the vestibulo-spinal reflexes and the balance motor control systems. A requisite component of this research effort includes the development of a computational model of the sensory-to-motor transformation relating the vestibular balance control system to its neural substrates. This model should be driven and validated by experimental data generated by this project. The Center is intended to support a team of investigators pursuing basic and applied studies at the systems and neuronal substrate levels to conduct an integrated, multidisciplinary inquiry into the vestibular bases of balance control.

The purpose of the research training component of the Center is to develop opportunities for training individuals to conduct research in the vestibular sciences. The research training program will provide multidisciplinary training for physicians, predoctoral trainees and postdoctoral trainees in the areas of vestibular science that are encompassed by the application. The research training component of the Center must provide opportunities for individuals with varying levels of research experience.

#### SPECIAL REQUIREMENTS

The program director and one additional investigator of the Center will meet annually in the Washington, DC area with the scientific program staffs of the Division of Communication Sciences and Disorders, NIDCD, and the Life Sciences Division, NASA, to review the progress of the Center in the areas of research and research training.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by November 15, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Center director, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDCD staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Earleen Elkins, Ph.D.  
Chief, Scientific Review Branch  
National Institute on Deafness and Other Communication Disorders  
Room 400-B, Executive Plaza South  
6120 Executive Boulevard  
Rockville, MD 20892

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone 301/496-7441; and from the NIH program administrator named below.

Applications must be received by December 15, 1992.

#### REVIEW CONSIDERATIONS

Incoming applications determined by NIH staff to be complete and responsive will undergo scientific merit review and a site visit or applicant interview in the Washington, DC area. These applications will be evaluated in accordance with the criteria stated in the RFA for scientific/technical merit by an appropriate peer review group convened by the Institute and NASA. The second level of review will be provided by the National Deafness and Other Communication Disorders Advisory Council and the NASA Life Sciences Division. If the number of applications received is large, the NIDCD may conduct a preliminary scientific peer review to eliminate those applications that are clearly not competitive.

#### AWARD CRITERIA

The anticipated date of award is July 1993.

Selection will be made jointly by the NIDCD and NASA on the basis of assessment of the applications by peer review, considerations of programmatic balance, and the appropriation of allocated funds for this RFA.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues and questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Daniel A. Sklare, Ph.D.  
Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-3461  
FAX: (301) 402-6251

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Grants Management Branch  
Division of Extramural Activities  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-0909  
FAX: (301) 402-1758

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## RESEARCH ON CLINICAL CARE IN NURSING HOMES

NIH GUIDE, Volume 21, Number 37, October 16, 1992

RFA AVAILABLE: NR-93-01

P.T. 34; K.W. 0785130, 0730050

National Center for Nursing Research

Letter of Intent Receipt Date: November 24, 1992

Application Receipt Date: January 26, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

### PURPOSE

The goal of this RFA is to enhance quality of care and quality of life of nursing home residents by increasing understanding of the influences of contextual factors and by determining clinical strategies that increase independence and self management among residents, maintain family participation in care, and encourage discharge to home whenever possible.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Research on Clinical Care in Nursing Homes, is related to the priority areas of older persons as a targeted group and to chronically disabling conditions. Potential applicants may obtain a copy of the "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit, public and private, organizations such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. Applicants must demonstrate access to nursing homes appropriate to the study proposed.

### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. This RFA is a one time solicitation. The total project period proposed may not exceed four years. The anticipated average direct cost of an award is \$150,000. The anticipated award date will be July 1, 1993.

### FUNDS AVAILABLE

It is estimated that up to \$1.0 million will be available to fund the first-year total costs of applications submitted in response to this RFA. It is anticipated that four to five applications will be funded.

### RESEARCH OBJECTIVES

1. Determine the influence of structural and organizational factors on the effectiveness of clinical interventions.
2. Examine the effectiveness of specific clinical interventions for older persons in nursing homes in terms of clinical quality (e.g., related to changes in functional status and quality of life) and related fiscal (e.g., related to changes in costs) outcomes.
3. Identify linkages among clinical assessments conducted in nursing homes, clinical interventions, and anticipated clinical and fiscal outcomes.

Applications must address objective one and either two or three.

### BACKGROUND

With the increasing longevity of our population, the number of the older persons is increasing, including those over 85 years who are frequent users of nursing homes. Many issues have been raised about the quality and appropriateness of clinical care provided in these settings. This RFA is designed to address these issues. There are several areas that could be addressed.

How best to assess and plan clinical interventions to meet individual requirements of nursing home residents needs to be addressed. The relationship of assessment strategies to clinical interventions and outcomes requires further investigation. Examinations are needed of potential differences among those with varying lengths of stay. Also, examinations are needed of clinical intervention strategies for residents who have the potential for discharge home, improvement in their health status, as well as those who are not expected to survive. It is important that the natural clinical setting be examined for influences on the effectiveness of intervention strategies, such as through exploration of clinical management strategies to achieve staff adherence to plans of care. In addition, clinical interventions that take the resident milieu into consideration continue to require study.



## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this inclusion must be provided. Applications without such documentation will not be accepted for review.

### LETTER OF INTENT

Prospective applicants are asked to submit, by November 24, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the names of other key personnel and consultants, the participating institution(s), and the number and title of the RFA in response to which an application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is extremely helpful in planning for the review of applications. It allows NCNR staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

Ethel Jackson, D.D.S.  
Chief, Office of Review  
National Center for Nursing Research  
Building 31, Room 5B25  
9000 Rockville Pike  
Bethesda, MD 20892

### APPLICATION PROCEDURES

Applications must be received by January 26, 1993. If an application is received after that date, it will be returned to the applicant without review. The research grant application form PHS 398 (rev. 9/91) is to be used to apply for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892 telephone 301-496-7441.

### REVIEW CONSIDERATIONS

Applications will be evaluated according to the review criteria stated in the RFA for scientific and technical merit by an appropriate peer review group convened by the Office of Review, National Center for Nursing Research. Applications may be subjected to triage by the peer review group to determine their scientific merit relative to other applications received in response to this RFA. Criteria for triage will be the same as those noted above. The second level of review will be provided by the National Advisory Council for Nursing Research.

### AWARD CRITERIA

The anticipated date of award is July 1, 1993. Decisions to make awards are based on the scientific merit of the application reflected in the priority score, availability of funds with NCNR for this purpose, and NCNR research program priorities.

### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged and may be directed to either of the following individuals. The program staff welcome the opportunity to clarify any issues or questions from potential applicants.

Patricia Moritz, Ph.D., R.N.  
Nursing Systems Branch  
National Center for Nursing Research  
Westwood Building, Room 754  
Bethesda, MD 20892  
Telephone: (301) 496-0523 (for copies of the RFA)  
Telephone: (303) 844-6163 (for scientific matters)

Direct inquiries regarding fiscal matters to:

Sally Nichols  
Grants Management Officer  
National Center for Nursing Research  
Westwood Building, Room 748  
Bethesda, MD 20892  
Telephone: (301) 496-0237

### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.331, Nursing Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

GENES DETERMINING STEM CELL SELF-RENEWAL AND COMMITMENT

NIH GUIDE, Volume 21, Number 37, October 16, 1992

PA NUMBER: PA-93-006

P.T. 34; K.W. 1002058, 0785070

National Heart, Lung, and Blood Institute

PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Program Announcement (PA) on the above subject. The purpose of this initiative is to encourage research aimed at providing an understanding of the genetic and molecular mechanisms responsible for controlling hematopoietic stem and progenitor cell self-renewal, commitment, and differentiation.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Genes Determining Stem Cell Self-Renewal and Commitment, is related to the priority areas of hematologic disorders and bone marrow transplantation. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-782-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. Awards in connection with this announcement will be made to foreign institutions only for research of very unusual merit, need and promise, and in accordance with PHS policy governing such awards. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) Awards (R29).

MECHANISM OF SUPPORT

This PA will use the National Institutes of Health (NIH) individual research grant (R01) and FIRST (R29) awards. Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project. Up to five years of support may be requested. Because the nature and scope of the research proposed in response to this PA may vary, it is anticipated that the size of an award will also vary. Applications for R29 awards may request no more than \$350,000 direct costs. Administrative adjustments in project period and/or amount of support may be required at the time of the award. All current policies and requirements that govern the research grant programs of the NIH will apply to grants awarded in connection with this PA.

RESEARCH OBJECTIVES

The purpose of this initiative is to encourage research aimed at providing an understanding of the genetic and molecular mechanisms responsible for controlling hematopoietic stem and progenitor cell self-renewal, commitment, and differentiation.

The production of blood cells, a process called hematopoiesis, takes place in the bone marrow. Hematopoiesis begins with the most primitive, pluripotent hematopoietic stem cell which is believed to be present as only one of every 1,000 to 100,000 nucleated bone marrow cells. The stem cell can either self-renew or differentiate into myeloid or lymphoid stem cells, which in turn can further differentiate and mature, ultimately giving rise to all the circulating blood cells. Each of these complex hematopoietic pathways is under the influence of one or more hematopoietic growth factors (colony stimulating factors) or cytokines that enhance cellular proliferation and maturation and other substances that exert negative or inhibitory effects on the process.

The past decade has witnessed the cloning and characterization of several hematopoietic growth factors. Many of these have already assumed a role in medical treatment. However, since these factors typically have more than one action, some of these actions may be undesirable in a given case. For example, some cytokines used to ameliorate chemotherapy-induced neutropenia may have the undesirable effect of stimulating the growth of tumor cells or of activating mature neutrophils. Hence, growth factors alone provide insufficiently precise control of the hematopoietic system.

Growth factors are only a part of a complex system regulating hematopoiesis. For each growth factor there is a receptor, signal transducers, and responsive genetic elements. Many of these receptors have been characterized; some can be the target of therapeutic attack through molecules designed to compete with their natural ligands. Much current work focuses on signal transduction. Intervention via signal transducers may be complicated by the fact that some signal transducers are common to several pathways serving different functions. Studies in several animal and cell culture systems support the idea that tyrosine kinase receptors, Ras and protein kinase C are part of a common signaling pathway. Thus, identification of responsive genetic elements for growth factors may be the best approach to obtain the specificity required for therapeutic intervention.

The hematopoietic stem cell and blood cell progenitors face a succession of "decisions," i.e., choices among alternative pathways. For example, between the quiescent stem cell and the mature neutrophil lie perhaps five

such decisions: (a) whether to remain quiescent or to divide; (b) if to divide, whether to remain multipotential (self-renew) or to restrict potentiality; (c) if to restrict potentiality, whether to become a lymphoid or a myeloid stem cell; (d) if to become a myeloid stem cell, whether to become an erythroid, megakaryocytic, or granulocytic progenitor; and (e) if to become granulocytic, whether to become a neutrophilic, eosinophilic, or basophilic progenitor. What these decisions represent at the molecular level, which result in commitment of multipotent progenitors to differentiate along a given lineage, remains elusive. The hypothesis behind this initiative is that each such decision represents activation of a set of genes via a "master" gene. The purpose of this initiative is to identify the genes responsible for the particular alternative pathways selected.

The concept of master genes in hematopoiesis has been advanced by studies using approaches in normal and transformed cell culture systems, isolation of multipotent cell lines derived from mouse bone marrow, and the use of hematopoietic cells transformed in vitro by oncogene-containing acute leukemia viruses. Alterations in gene expression can have profound effects on the growth and differentiation of hematopoietic cells. Thus, it is important to understand the mechanisms by which various genes are regulated during hematopoietic cell differentiation. There is some evidence to suggest that the decision for myeloid differentiation rather than for lymphoid differentiation may involve expression of the *myb* gene (1). Thus, *myb* may play a key regulatory role in myeloid differentiation and also play an important role in leukemogenicity (2). The decision for erythropoiesis rather than for granulopoiesis or megakaryocytopoiesis may involve expression of the *ets* gene. However, it was recently shown that the immature chick "erythroid" cells transformed by the E26 avian leukemia virus are in fact multipotent progenitors and can differentiate along at least three lineages (3). It is important to determine if mammalian counterparts exist and have similar functions, particularly in man. This approach was successful in the use of chicken and mouse genes to identify the human counterpart of a transcription factor gene (*GATA*) required for normal differentiation of erythroid cells (4). The gene for the *GATA* protein has been cloned which has led to the identification of a family of *GATA* proteins expressed in different tissues. Similarly, genes of the *HOX* 2 cluster of homeobox genes have been identified in human hematopoietic cell lines with erythroid potential, suggesting that these genes are involved in human hematopoietic cell differentiation. Overexpression of *HOX* 2.2 is associated with loss of erythroid features and an increase in certain myelomonocytic markers (5). This strategy can generally be applied to differentiation of other lineages, provided that several proteins specific for that lineage have been identified.

The second approach, starting with a candidate gene, is also feasible. As discussed above, an attractive class of genes are the proto-oncogenes, many of which were discovered through their mutated form in tumor viruses. Their unmutated forms must perform important functions because they have been preserved over the course of eukaryotic evolution. A plausible normal function for them is the regulation of cellular proliferation and differentiation. Once a gene is selected for study, its role can be investigated by blocking its effect using antisense technology. This approach has been successfully used in several systems in which it provides a new strategy for inducing differentiation and also provides further insight into the molecular factors that govern the process of hematopoiesis (6,7,8).

These approaches are intended to serve as examples and other novel approaches to address the molecular mechanisms for lineage commitment are encouraged. An attack upon these fundamental problems in hematopoiesis is now possible due to progress in isolating hematopoietic stem cells and defining the requirements for their culture. The hypothesis behind this initiative is that each decision made by a cell (to divide or not to divide; to divide and self-renew or commit, etc.) represents activation of a set of genes via a "master" gene. The purpose of this initiative is to identify these master genes by encouraging research aimed at providing an understanding of the genetic and molecular mechanisms responsible for controlling hematopoietic stem and progenitor cell self-renewal, commitment, and differentiation.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans including American Indians or Alaskan Natives, Asian/Pacific Islanders, Blacks, and Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.



For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 (rev. 9/91) instructions.

FIRST Award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. Section 2a on the face page of the application must be completed. Check "YES" to indicate the application is submitted in response to a program announcement. The title and program announcement number must be typed in Section 2a of the application as follows: "GENES DETERMINING STEM CELL SELF-RENEWAL AND COMMITMENT" NHLBI PA NUMBER: PA-93-006.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Although this is a National Heart, Lung, and Blood Institute PA, the National Institute of Diabetes and Digestive and Kidney Diseases also has an interest in the subject matter of this PA. Applications will be assigned to the most appropriate Institute on the basis of established Public Health Service referral guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard peer review procedures.

Following scientific-technical review, the applications will receive a second-level review by the appropriate National Advisory Council.

#### AWARD CRITERIA

Funding decisions will be made on the basis of scientific and technical merit of the proposed grant as determined by peer review, program needs and balance among research areas of the announcement, and the availability of funds.

Awards in response to this PA will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with PHS policy governing such awards.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues and questions from potential applicants is welcome.

Inquiries regarding this request for applications may be directed to:

Dr. Helena O. Mishoe  
Cellular Hematology Branch  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Federal Building, Room 5A12  
Bethesda, MD 20892  
Telephone: (301) 496-5911  
FAX: (301) 496-9940



For fiscal and administrative matters, contact:

Ms. Jane R. Davis  
Chief, Blood Division Grants Management Section  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A15  
Bethesda, MD 20892  
Telephone: (301) 496-7257  
FAX: (301) 402-1200

#### AUTHORITY AND REGULATIONS

The programs of the Division of Blood Diseases and Resources, NHLBI, are described in the Catalog of Federal Domestic Assistance number 93.839. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372.

#### REFERENCES

1. Selvakumaran, M., Liebermann, D.A., Hoffman-Liebermann B. Deregulated c-myc disrupts interleukin-6- or leukemia inhibitory factor-induced myeloid differentiation prior to c-myc: role in leukemogenesis. (1992) Mol Cell Biol 12:2493-500.
2. Graf, T. Myb: a transcriptional activator linking proliferation and differentiation in hematopoietic cells. (1992) Curr Opin Genet 2:249-55.
3. Graf, T., McNagny, K., Brady, G., Frampton, J. Chicken "erythroid: cells transformed by the Gag-Myb-Ets-encoding E26 leukemia virus are multipotent. (1992) Cell 24:201-13.
4. Pevny, L., Simon, M.C., Robertson, E., Klein, W.H., et al. Erythroid differentiation in chimeric mice blocked by a targeted mutation in the gene for transcription factor GATA-1. (1991) Nature 349:257-60.
5. Shen, W. F., Detmer, K., Mathews, C. H., Hack, F. M., et al. Modulation of homeobox gene expression alters the phenotype of human hematopoietic cell lines. (1992) EMBO J 11:983-9.
6. Catlett, J. P., Leftwich, J. A., Westin, E. H., Grant, S., Huff, T. F. c-kit expression by CD34+ bone marrow progenitors and inhibition of response to recombinant human interleukin-3 following exposure to c-kit antisense oligonucleotides. (1991) 78:3186-91.
7. Wu, J., Zhu, J. Q., Zhu, D. X., Scharfman, A., et al. Selective inhibition of normal murine myelopoiesis in vitro: by a Hox 2.3 antisense oligodeoxynucleotide. (1992) Cell Mol Biol 38:367-76.
8. Collins, J. F., Herman, P., Schuch, C., Bagby, G. C. c-myc antisense oligonucleotides inhibit the colony-forming capacity of Colo 320 colonic carcinoma cells. (1992) J Clin Invest 89:1523-7.

#### INSTITUTIONAL TRAINING AWARDS IN NUTRITIONAL SCIENCES

NIH GUIDE, Volume 21, Number 37, October 16, 1992

PA NUMBER: PA-93-007

P.T. 44; K.W. 0720005, 0710095, 0715145, 0765020

National Institute of Diabetes and Digestive and Kidney Diseases

#### PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites applications for National Research Service Award (NRSA) institutional grants (T32) from eligible institutions to develop or enhance research training for predoctoral students or postdoctoral fellows, selected by the institution, in the broad areas of nutritional science and obesity-related research. The purpose of this NRSA program, and this announcement, is to ensure a cadre of well-trained scientists interested in pursuing academic research careers in the areas of nutrition, nutrient metabolism, eating disorders, obesity, and energy metabolism/regulation. Other Institutes and Centers share an interest in these disorders. Assignment of applications to components of the National Institutes of Health will be according to standard Public Health Service (PHS) referral guidelines.

To ensure a fully adequate review, applications submitted in response to this announcement and assigned to the NIDDK will be reviewed only annually in the review cycle, ending with presentation to the National Diabetes and Digestive and Kidney Diseases Advisory Council at its September/October meeting. Therefore, it is requested that applications be submitted for the January 10 receipt date of each year. This applies both to new applications and to competing continuation applications in the area of nutritional sciences. NIDDK-assigned applications submitted for the other receipt dates of May 10 and September 10 will be held for review with those submitted on the following January 10.

The PHS is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Institutional Training Awards in Nutritional Sciences, is related to the priority area of nutrition. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic non-profit private and public institutions to support research training programs. The applicant institution must have, or be able to develop, the staff and facilities required for the proposed program. The training program director at the institution will be responsible for the selection and appointment of trainees to receive support and for the overall direction of the program.

The individuals to be trained on an NRSA training grant must be citizens or non-citizen nationals of the United States or have been lawfully admitted for permanent residence (i.e., in possession of the Alien Registration Receipt Card I-551 or I-151) at the time of appointment. Individuals on temporary or student visas are not eligible. NRSA research training grants may not be used to support studies leading to the M.D., D.O., D.D.S., D.V.M., or other similar health-professional degree.

Programs able to provide postdoctoral training to both M.D.s and Ph.D.s are encouraged.

#### MECHANISM OF SUPPORT

The mechanism of support for this program announcement will be the National Research Service Award institutional training grant (T32). Institutions may request support for predoctoral students, postdoctoral trainees, and short-term research training. Stipends will be awarded at levels commensurate with NIH policy at the time of award and may be supplemented from non-Federal sources. Training related expenses, tuition and fees, and travel expenses may also be requested for trainees, although the levels vary depending on the type of training to be supported. Trainees should be appointed to postdoctoral positions for at least two years. Indirect costs will be awarded based on eight percent of total direct costs with no exclusions from the base for training-related expenses. It is anticipated that the size of awards will vary, possible ranging up to \$250,000 per year.

#### RESEARCH OBJECTIVES

The NIDDK is committed to increasing the number of well-trained physicians and basic scientists interested in conducting high quality research in areas of nutritional science and able both to compete successfully for NIH grant support and provide leadership in the areas of clinical nutrition/obesity research.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91). Application kits are available from most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of this announcement must be typed in section 2a on the face page of the application.

Prior to preparing an application, prospective applicants should consult the following documents: (a) "National Research Service Award Guidelines for Individual Awards - Institutional Awards" available from most grantee offices of sponsored research and from the Office of Grants Inquiries at the address listed above; and (2) "Suggestions for National Research Service Award Institutional Training grant Applications" available from the Review Branch, National Institute of Diabetes and Digestive and Kidney Diseases, Westwood Building, Room 604, Bethesda, MD 20892, telephone (301) 496-7083.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Preferably, applications should be received on or before the January 10 receipt date.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed initially by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration.

All applications responding to this announcement that are assigned to the NIDDK will be reviewed for scientific and technical merit by the DDK-C initial review group (IRG), followed by a second level review by the National Diabetes and Digestive and Kidney Diseases Advisory Council. Applications not recommended for further consideration by the IRG will not undergo secondary review. Applications assigned to Institutes/Centers other than the NIDDK will undergo a similar 2-level review process within the designated Institute/Center.

Initial review of applications assigned to the NIDDK will be held in June or July of each year, and review by the National Diabetes and Digestive and Kidney Diseases Advisory Council will be in September or October. Review criteria used by initial review groups in reviewing NRSA Institutional Training applications are given in the booklet "National Research Service Award Guidelines for Individual Awards - Institutional Awards" available from the Office of Grants Inquiries at the address listed under APPLICATION PROCEDURES.

## AWARD CRITERIA

Applications will compete for available funds with other approved applications. The following will be considered in making funding decisions:

- o scientific and technical merit of the application as determined by peer review
- o availability of funds
- o program balance

## INQUIRIES

Inquiries regarding programmatic issues may be directed to:

Judith M. Podskalny, Ph.D.  
Director, Research Training and Career Development Program  
Division of Digestive Diseases and Nutrition  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A15  
Bethesda, MD 20892  
Telephone: (301) 496-7455

Inquiries regarding fiscal matters may be directed to:

Mrs. Paulette Badman  
Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.848. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 66 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ACADEMIC AWARD IN VASCULAR DISEASE

NIH GUIDE, Volume 21, Number 37, October 16, 1992

PAR NUMBER: PAR-92-008

P.T. 34; K.W. 0715040, 0710030

National Heart, Lung, and Blood Institute

Application Receipt Date: January 7, 1993

## PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) announces the third national competition for Academic Awards in Vascular Disease. These awards have the dual purpose of encouraging the development and/or improving the quality of clinical, educational, and research programs in vascular disease and of encouraging the professional development of the Awardee so that he or she can serve as the focal point for multidisciplinary interactions in the field of vascular medicine.

## HEALTHY PEOPLE 2000

The Public Health Service is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement, Academic Award in Vascular Disease, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Each school of medicine or osteopathy in the United States and its possessions and territories is eligible to compete for a nonrenewable Academic Award in Vascular Disease for a project period that does not exceed five years. Awards will not be made to foreign institutions nor to domestic applicants with international components. The Principal Investigator must hold the M.D. or D.O. degree or the equivalent. Applications from minority individuals and women are encouraged. An individual institution may submit an application for a systemic vascular program and an application for a pulmonary vascular program for a given receipt date. However, an individual institution applying for a comprehensive systemic and pulmonary vascular program in a single application may submit only one application for a given receipt date. The number of new awards made each year will depend on the availability of funds.



## MECHANISM OF SUPPORT

The mechanism of support for this program is the Academic/Teacher Award (K07).

## RESEARCH OBJECTIVES

This Academic Award is initiated to address problems that prevent rapid and effective application of new developments in medical diagnosis and care of the individual patient. Major reasons for inefficient transfer of new technology to patients with vascular disease relate to the rapid advance of basic and clinical research as well as to the absence of a specific specialty dedicated to such patients. Thus, the purpose of this Academic Award is to provide financial support for individuals applying, in conjunction with their institutions, to develop and implement approaches to the coordinated care of patients with vascular disease in need of a variety of specialty and subspecialty expert consultation. In conjunction with this program, it is also expected that complementary educational and research programs will be developed or are already in place.

For the purposes of this Award, vascular medicine is defined as the clinical discipline that has as its objectives: (1) clinical characterization, (2) pathogenesis, (3) diagnosis, (4) treatment, and (5) prevention of systemic and/or pulmonary vascular disease. To be responsive to this announcement, an application must provide for a program in systemic or pulmonary vascular disease or a comprehensive program in both. A systemic vascular program should include cerebral, coronary, aortic, renal, peripheral and lymphatic circulations and address such disorders as atherosclerosis, lipid metabolic disorders, hypertension, lymphedema, thrombosis, vasculitis and vasospastic disorders. A pulmonary vascular disease program should include primary and secondary pulmonary hypertension, pulmonary vasculitis and pulmonary thromboembolism.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders or conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully. Since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer review will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in the priority score assigned to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

## APPLICATION PROCEDURES

Prospective applicants are asked to submit, by November 20, 1992, a letter of intent, countersigned by the applicant's Department Chairman, Dean of the School of Medicine or Osteopathy, and Director of the hospital(s). This letter of intent should include a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the program announcement in response to which an application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of



subsequent applications, the information that it contains allows NHLBI staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

C. James Scheirer, Ph.D.  
Chief, Contracts, Clinical Trials, and Training Review Section  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 548  
Bethesda, MD 20892  
Telephone: (301) 496-7363

Applications for the Academic Award in Vascular Disease must be received no later than January 7, 1993, by the NIH for review by the National Heart, Lung, and Blood Advisory Council in May 1993. The requested start date for funding should be July 1, 1993.

Applications are to be submitted on the traditional research grant application form PHS 398 (rev. 9/91). The form is available in an applicant institution's office of sponsored research or business office and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7447. Use the conventional format for research grant applications and ensure that the points identified in the section "INSTRUCTIONS FOR PREPARING APPLICATIONS" are fulfilled. Applicants are expected to conform to the 25-page limit as directed in the application kit (PHS 398). Appendices containing supporting materials may be submitted with the application, but may not be used to circumvent this requirement.

Send or deliver an original completed application and three signed, exact photocopies to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the same time, applicants must also send two additional copies of the application to Dr. James Scheirer at the address listed above.

Applications must be received by January 7, 1993, for review at the May 1993 meeting of the National Heart, Lung, and Blood Advisory Council. Awards will be made with a beginning date of July 1, 1993.

#### REVIEW PROCEDURES

The primary technical review of applications will be by a special review group managed by the Division of Extramural Affairs, NHLBI, predominantly composed of non-federal scientists with expertise in various areas of systemic and pulmonary vascular disease. The review will include an initial assessment of the written application based on the Objectives and Criteria for the Award in the Guidelines. Guidelines may be requested from individuals named below under INQUIRIES.

Prospective Awardees whose applications are determined to be competitive will be invited for an interview in Bethesda, Maryland. Travel expenses for this interview must be paid by the applicant institution. When necessary, a site visit may be made to the institution to determine the institutional environment, the commitment of the sponsoring division or department head and director of the hospital, and evidence of cooperation that may be needed to implement the candidate's proposed program. Following scientific- technical review, the applications will receive a second level review by the National Heart, Lung, and Blood Advisory Council.

#### AWARD CRITERIA

Criteria for the award include the ability of both the sponsoring institution and the candidate to implement a program based on the objectives of the Academic Award. Awards will also be dependent on the availability of funds.

#### INQUIRIES

To receive the full set of Guidelines and to clarify questions related to applicant eligibility and appropriate areas of emphasis, contact any of the following:

Carol H. Letendre, Ph.D.  
Associate Director for Scientific Programs  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Federal Building, Room 516  
Bethesda, MD 20892  
Telephone: (301) 496-8966

David M. Robinson, Ph.D.  
Associate Director for Scientific Programs  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 416B  
Bethesda, MD 20892  
Telephone: (301) 496-5656

Carol Vreim, Ph.D.  
Associate Director for Scientific Program Operation  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 6A16C  
Bethesda, MD 20892  
Telephone: (301) 496-7208

Direct inquiries regarding fiscal matters to:

Mrs. Marie A. Willett  
Deputy Chief, Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung and Blood Institute  
Westwood Building, Room 4A12  
Bethesda, MD 20892  
Telephone: (301) 496-7255



#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.837, 93.838, and 93.839. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

5333 Westbard Avenue  
Bethesda, MD 20816

# NIH GUIDE

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## For Grants and Contracts

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**National Institutes of Health Room B4BN23,**  
**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 38, Part I of II  
October 23, 1992

RICHARD W MURRY

\* 340189  
\*\*51350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

# NOTICES

## NIH REGIONAL CONFERENCE IN GRANTS ADMINISTRATION

NIH GUIDE, Volume 21, Number 38, October 23, 1992

P.T. 42; 1014006

National Institutes of Health

A regional conference covering topics related to grants administration at the National Institutes of Health (NIH) has been scheduled for Thursday through Friday, January 14-15, 1993, at the San Diego Marriott - La Jolla in La Jolla, California. La Jolla is a beautiful coastal community, located just 20 minutes from Lindbergh Field, San Diego's International Airport.

The conference, hosted by the University of California, San Diego, is located to attract research administrators from the western region of the United States--Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, North Dakota, Oregon, South Dakota, Utah, Washington, and Wyoming. Those interested from other states are encouraged to attend. In addition, staff from small and minority colleges, for-profit research organizations, hospitals, universities, and research institutes and centers are also invited.

This two-day conference will be of interest to both new and senior grants administrators and principal investigators. Discussions of current issues that affect NIH funding and grants administration are included to give conference participants a comprehensive, up-to-date view of NIH-sponsored research. Topics for discussion will include the fundamentals in conducting business with NIH (application preparation, peer review, budget analysis, and award determination), and contemporary topics (strategic and financial management plan, indirect cost, and administrative effectiveness between NIH and recipients). The format for this conference will include case studies, group discussions, and formal presentations. Time will be available for conference participants to meet informally with NIH representatives and discuss topics of special interest.



Mr. Geoffrey Grant, Grants Policy Officer in the Office of Extramural Research at NIH, and outstanding representatives from the Division of Research Grants, grants management, and program staff of several awarding components of NIH will be featured speakers.

DATE: January 14-15, 1993

LOCATION:

San Diego Marriott - La Jolla  
4240 La Jolla Village Drive  
La Jolla, CA 92037  
Telephone: (619) 587-1414

REGISTRATION AND INQUIRIES:

Advance registration is required by December 9, 1992, as conference space is limited to the first 250 registrants. For registration information, contact:

Ms. Jeaneth Villegas  
Telephone: (619) 534-2972  
Fax: (619) 534-0280

COST OF WORKSHOP:  
\$125

INVENTIONS - REPORTS, ROYALTY INCOME, AND RELATED MATTERS: IMPORTANT NOTICE FOR INVESTIGATORS AND OFFICIALS RESPONSIBLE FOR PATENT MATTERS

NIH GUIDE, Volume 21, Number 38, October 23, 1992

P.T. 34; K.W. 1014006

Public Health Service

This notice directs the attention of recipients of PHS research grants, contracts, and cooperative agreements to certain terms of these awards that protect the public's interest in inventions made with Federal assistance. (The term recipient will apply to both grantees and contractors.)

**EMPLOYEE/EMPLOYER RESPONSIBILITIES:** Acceptance of grant or contract funds obligates recipients to comply with the "standard patent rights" clauses at 37 CFR 401.14 or FAR 52.227-11. So that recipients can comply with the reporting provisions of Paragraph (c) of these clauses, Paragraph (f) - "Contractor Action to Protect the Government's Interest," among other things, directs recipient institutions to require, by means of a written agreement, their employees, other than clerical and nontechnical employees, to disclose promptly inventions made with Federal assistance to the recipient official responsible for patent matters. Further, through employee agreements or educational programs, recipients are required to instruct such employees on the importance of reporting such inventions in sufficient time to permit the filing of patent applications prior to U.S. or foreign statutory bars. Additional guidance on recipient reporting requirements for inventions can be found in the NIH Guide for Grants and Contracts, Vol. 19, No. 23, June 22, 1990, and the PHS Grants Policy Statement, page 8-22 (rev. 9/1/91). Note: Inventions made with NIH (or former ADAMHA) funds should be reported to the Extramural Inventions Office at the address shown below, whereas inventions made with funds from other PHS agencies should be reported to that agency's Grants Management Officer or Contracting Officer.

**SUBCONTRACTS UNDER GRANTS AND CONTRACTS:** Recipients must include, at least by specific reference, the Standard Patent Rights clause of 37 CFR 401.14 or FAR 52.227-11, as appropriate, in all contracts or sub-contracts under grants and contracts for experimental, developmental, or research work, regardless of tier.

**UTILIZATION REPORTS vis-a-vis FINANCIAL STATUS REPORTS:** Questions have arisen regarding interpretation of language concerning grant-related income in Chapter 8 of the PHS Grants Policy Statement, or more particularly in the Department's regulations, 45 CFR 74, Subpart F. There, patent and copyright royalty income is included as a portion of "program income." In turn, Subpart I requires reporting of "program income" on the annual Financial Status Report for each project. The PHS has agreed that for the special case of patent and invention royalties the preferred reporting channel, and the one that meets the requirements of Subpart I, is the annual utilization report of subject inventions authorized by 35 U.S.C. 202(c)(5), 37 CFR 401.14(h), and FAR 52.227-11(h). Such reports by recipients and their licensees or assignees shall contain information regarding the status of development, date of first commercial sale or use, and gross royalties received by the recipient. Recipients may develop their own, simplified format for these reports. This information shall be treated as confidential, privileged information, not subject to disclosure under the Freedom of Information Act without permission of the recipient.

Previous issues of the NIH Guide for Grants and Contracts, February 9 and June 22, 1990, specified a biennial reporting cycle. In view of the foregoing discussion, recipients are hereby directed to institute the utilization reporting process on an annual basis. Since these reports are being submitted to the funding agency, there is no requirement for additional, separate reporting to the Department of Commerce as some have done in the past.

**NOTE:** Utilization reports are required ONLY for licensed inventions that have generated royalty or licensing income.

**COPYRIGHT ROYALTY INCOME:** If a Notice of Grant Award specifies that the deductive or matching option must be used for the disposition of copyright royalty income, such income must be reported on the Financial Status Report. Utilization reports are not required for copyrighted material.

**ACKNOWLEDGEMENT OF FEDERAL SUPPORT:** Recipients are required to include within the specification of any U.S. patent application and any patent issuing thereon the following statement, "This invention was made with government support under (identify the grant or contract) awarded by the PHS. The government has certain rights in the invention."

**ROYALTY-FREE SALES:** By law, the Federal Government has a royalty-free license to practice the subject inventions for or on its behalf. Thus, when licensing staff of the recipient institution are drafting commercial licenses they should exercise care and include a provision for this license to the Government.

**COMPLIANCE:** Failure to comply with requirements of the "patent rights clause" can result in loss of the recipient's rights in inventions, (37 CFR 401.14(d), or FAR 52.227-11(d)).

**INQUIRIES AND RECEIPT POINT FOR NIH UTILIZATION REPORTS:**

Howard P. Jenerick, Ph.D.  
Extramural Inventions Office  
National Institutes of Health  
Building 31, Room 5B41  
Bethesda MD 20892  
Telephone: (301) 402-0850  
FAX: (301) 496-0166

**APPLICATION RECEIPT DATES AND THE REVISED PHS 398: A REMINDER**

NIH GUIDE, Volume 21, Number 38, October 23, 1992

P.T. 34; K.W. 1014006

National Institutes of Health

The National Institutes of Health (NIH) guidelines governing receipt dates for applications have not changed and may be found on page 4-14 of the PHS Grants Policy Statement (rev. 9/91). Item 2 in the first full paragraph in the instructions on page 8 of the revised PHS 398 application (rev 9/91) is applicable to PHS agencies and programs that do not utilize the NIH Division of Research Grants (DRG).

For grant applications processed through NIH, DRG, the Division of Research Grants system requires that applications must be RECEIVED by the published application receipt dates. However, an application received after the deadline may be acceptable if it carries a legible proof-of-mailing date assigned by the carrier and the proof-of-mailing date is not later than one week prior to the deadline date.

**ADAMHA/NIH REORGANIZATION**

NIH GUIDE, Volume 21, Number 38, October 23, 1992

P.T. 34; K.W. 1014006

National Institutes of Health

The three institutes that formerly comprised the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) became part of the National Institutes of Health (NIH) on October 1, 1992. Henceforth, whenever used in the NIH Guide for Grants and Contracts, the term "NIH" refers to the following organizational entities:

Office of the Director  
National Institute on Aging  
National Institute of Alcohol and Alcoholism  
National Institute of Allergy and Infectious Diseases  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
National Cancer Institute  
National Institute of Child Health and Human Development  
National Institute on Deafness and Other Communication Disorders  
National Institute of Dental Research  
National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute of Drug Abuse  
National Institute of Environmental Health Sciences  
National Eye Institute  
National Institute of General Medical Sciences  
National Heart, Lung and Blood Institute  
National Institute of Mental Health  
National Institute of Neurological Disorders and Stroke  
National Library of Medicine  
National Center for Human Genome Research  
National Center for Nursing Research  
National Center for Research Resources  
Fogarty International Center  
Division of Computer Research and Technology  
Division of Research Grants

## INQUIRIES

Ms. Myra Brockett  
Institutional Affairs Office  
Building 31, Room 5B31  
Bethesda, MD 20892  
Telephone: (301) 496-5366

## NOTICES OF AVAILABILITY (RFPs AND RFAs)

### INITIATIVE FOR MINORITY STUDENTS: BRIDGES TO THE DOCTORAL DEGREE

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA: GM-93-001

P.T. 44, FF; K.W. 0720005, 0710030

National Institute of General Medical Sciences

Letter of Intent Receipt Date: November 20, 1992

Application Receipt Date: January 6, 1993

#### PURPOSE

The National Institute of General Medical Sciences (NIGMS) and the Office of Minority Programs (OMP), National Institutes of Health (NIH), solicit applications for two new initiatives directed at increasing the number of underrepresented minorities entering careers in biomedical research. The programs target two different underrepresented minority student populations: those in colleges and universities offering only Master of Science (M.S.) degree programs in biomedically-related sciences and those in two-year junior or community colleges. These have been identified as two key transition points for students considering careers in biomedical research. These initiatives seek to encourage the development of new and innovative programs and the expansion of existing programs to improve the academic competitiveness of underrepresented minority students and facilitate their transition into the next stage towards careers in biomedical research.

This Request for Applications (RFA) solicits applications for a partnership program involving institutions awarding the Master's degree and universities awarding the Ph.D. degree. A separate RFA (GM-93-002) describes a program targeting the transition from two-year colleges awarding the Associate's degree to institutions awarding the Baccalaureate degree.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, private and public, educational institutions and by state and local systems of higher education. Institutions that have already received NIGMS Bridge Program awards (R25) are not eligible to apply for this RFA.

An institution or system of higher education may submit ONLY ONE application for this RFA. Institutions that submit applications in response to this RFA may also apply for RFA GM-92-002; however, a separate application for each RFA is required. Institutions submitting their own applications may participate in programs with other applicant institutions so long as these interactions are consistent with institutional resources and the unified institutional plans described in BOTH applications (see Unified Plan under SPECIAL REQUIREMENTS). If an institution is involved in more than one application, justification should be provided for each.

Programs developed or modified under this initiative must be specifically designed to target underrepresented minority graduates majoring in the sciences. For purposes of this announcement, underrepresented minority students are individuals belonging to a particular ethnic or racial group that has been determined by the grantee institution to be underrepresented in biomedical or behavioral research. Nationally, individuals who have been found to be underrepresented in biomedical or behavioral research include, but are not limited to, Black Americans, Hispanic Americans, Native Americans and Pacific Islanders. The term "science" is used in this RFA to mean biomedical or health-related science.

Applications must include a partnership between an institution that offers the M.S. degree as the only postgraduate degree in the sciences within the participating departments AND has a significant enrollment of underrepresented minorities, and one research university providing Ph.D. degree programs in areas relevant to the biomedical sciences.

All applications must involve a partnership of at least two colleges or universities, but may involve a consortium of several institutions, and may include several institutions within a single state system. One participating institution or a single system of higher education must be designated as the grantee institution and must submit the application. The grantee institution must name the program director. Each participating institution must name one individual to act as program coordinator for that institution. Proposals must include a description of the collaborative arrangement with all participating institutions.

Institutions offering both the M.S. and Ph.D. degrees may not use funds from this program for graduates of their own M.S. degree programs to enter their own Ph.D. degree programs, even if the student is moving from one department, school, or college to another. The program seeks to promote and enhance partnerships BETWEEN institutions.

For additional requirements see SPECIAL REQUIREMENTS.



## General

Awards under this RFA will use the institutional education project (R25) grant. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed two years. Requested direct costs are not to exceed \$300,000 for the two-year period. Indirect costs will be paid at 8 percent of the direct costs minus appropriate exclusions. A detailed budget for each year must be provided.

This RFA is a one-time solicitation. Future unsolicited competing applications will not be accepted.

## Allowable Costs

If appropriate, the budget request may be divided into two phases: a planning phase with its attendant budget for the development of the partnership program; and an implementation phase with its attendant budget. The planning phase costs should be minimal and not exceed a period of one year. Faculty release time for planning and implementation of the program and faculty travel related to program development may be requested.

The implementation phase may include the costs of administering and coordinating the partnership programs within and between each of the participants. Although compensation for student participation in research experiences may be requested, stipends, housing, tuition, and fees are not allowable costs under this program. However, salary/wages, tuition remission and other forms of compensation paid in lieu of wages to students performing necessary work are allowable provided there is an employer-employee relationship between the student and the institution, the total compensation is reasonable for the work performed, and it is the institution's practice to provide compensation for all students in similar circumstances, regardless of the source of support for the activity. Requests for equipment, supplies, travel, and other expenses should be limited to those necessary for program development and should be carefully and specifically justified.

## FUNDS AVAILABLE

The funds for this program are contingent on the final level of the Fiscal Year 1993 appropriations to the OMP. An estimated \$7 million will be available in Fiscal Year 1993 for supporting awards made in response to RFA GM-92-001 and RFA GM-92-002. NIH staff anticipate making a combined total of 20 to 40 two-year awards for both RFAs using multi-year funding, if NIH receives sufficient numbers of highly meritorious applications and sufficient funds for this purpose.

## OBJECTIVES

## Background

This program seeks to promote the initiation and development of new transitional programs, as well as the expansion and enhancement of existing programs between those institutions with departments offering only the M.S. degree as the post-graduate academic degree in the sciences, which have significant enrollments of underrepresented minority students, and research universities with Ph.D. degree programs. The objective is to facilitate the transition of underrepresented minority students into Ph.D. programs after obtaining the M.S. degree. Students receiving the M.S. degree in one field of science may pursue the Ph.D. in a different area so long as the Ph.D. is in a discipline related to the biomedical sciences.

Collaborative agreements should take the form that best fits the needs and situations of the institutions involved. The challenge for the project director, with the help of the participating partners, is to design a new partnership program, or enhance an existing program, that will focus attention and adequate resources to the M.S. degree-granting institutions to enhance the academic competitiveness of their degree programs and graduates in the sciences.

## Additional Information

The "bridge" programs must be designed with special attention to the needs and special requirements of the underrepresented minority student body. They may include, but are not limited to, the following elements:

- o providing research opportunities for M.S. students at the Ph.D. institution or in private industrial laboratories (students may receive compensation for these activities);
- o establishing a mentoring program for M.S. students with faculty at the Ph.D. institution;
- o strengthening the research capability of the M.S.-granting college (e.g., by faculty research collaborations, joint seminar programs, etc.);
- o enhancing the curriculum of the M.S. institution (special courses, seminars, etc.);
- o enabling and encouraging students from either institution to take classes at the other institution;
- o guaranteeing acceptance into the participating Ph.D. program(s) for students completing the M.S. program;
- o academic counseling for M.S. students, with a particular focus on encouraging students to pursue research careers in the biomedical sciences.

It is an expectation of NIGMS and OMP that students who enter Ph.D. programs as a result of this enhancement program will receive institutional support, if needed, while progressing satisfactorily in Ph.D. research training programs. Applicants should describe the type(s) of institutional support that would be available to such students.



## SPECIAL REQUIREMENTS

Applicants should describe fully the proposed transition program and explain how its design will meet the goals of this initiative. Applicants with an existing transition program should describe that program and explain how it would be altered to meet the goals of this initiative.

### Unified Plan

To avoid duplication of effort each institution should develop a unified plan (which may include the biomedically relevant physical, natural and/or behavioral sciences) to facilitate the transfer of its students from the M.S. degree program to the Ph.D. degree program at another institution. Applicants should describe how this proposal fits in with the institution's overall transition plan.

### Consortium Agreements

Each applicant institution should delineate appropriate agreements and consortium arrangements with other institutions consistent with its own unified institutional plan. The following statement, accompanied by signatures of the appropriate administrative officials from EACH of the collaborating institutions, must be included as part of the application:

"THE APPROPRIATE PROGRAMMATIC AND ADMINISTRATIVE PERSONNEL OF EACH INSTITUTION INVOLVED IN THIS GRANT APPLICATION ARE AWARE OF THE NIH CONSORTIUM GRANT POLICY AND ARE PREPARED TO ESTABLISH THE NECESSARY INTER-INSTITUTIONAL AGREEMENT(S) CONSISTENT WITH THAT POLICY."

In addition, letters, signed by the appropriate institutional official and program coordinator, acknowledging participation in the program are required from each participating institution.

### Reporting Requirements

A progress report will be required at the end of the planning phase (if any) or at the end of the first year, whichever is shorter. A final report will be required 90 days after the termination date of the award and must include a Statement of Appointment Form (form 2271) for each student participant as well as a report of the benefits to students of the partnership program.

### Student Population and Career Tracking

The nature and extent of underrepresented minority student participation must be thoroughly delineated. The applicant should also describe the M.S. degree-granting institution's success in training its students in the sciences, including information on the numbers of minority students receiving the M.S. degree and data on subsequent careers or education of their graduates.

The applicant should describe a system by which it would monitor and track the students participating in this program, including their future careers, in order to evaluate the success of the program.

### Other Training Programs

Colleges with any NIH funding such as the Minority Access to Research Careers (MARC), Minority Biomedical Research Support Program (MBRS), National Research Service Award (NRSA) training grants, and/or project grants, or other sources of funds such as National Science Foundation grants or Howard Hughes grants, should define the relationship between those programs and this transition program. They should delineate how this enhancement program will influence their partnerships with the other participants and the manner in which underrepresented minority students in the transition program will interact with these other sources of support.

## LETTER OF INTENT

Prospective applicants are requested to submit, by November 20, 1992, a letter of intent that includes a descriptive title of the proposed plan, the name, address, and telephone number of the program director, the identities of other key personnel and participating institutions, and the number and title of the RFA. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIH staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Americo Rivera, Jr., Ph.D.  
National Institute of General Medical Sciences  
Westwood Building, Room 909  
Bethesda, MD 20892  
Telephone: (301) 496-7001  
FAX: (301) 402-0019

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441; and from the NIGMS program administrator named below.

The RFA label in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the

review committee in time for review. In addition, the RFA number and title must be typed on line 2A of the face page form, the "YES" box must be marked, and "R25" typed in 2B.

Submit a signed, typewritten original of the application, including the Checklist, and three photocopies of the signed application in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies of the application must also be sent to Dr. Americo Rivera, Jr. at the address given below.

Applications must be received by January 6, 1993. Applications arriving after that date will be returned to the applicant.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be administratively reviewed by NIH staff. Incomplete and/or unresponsive applications will be returned to the applicant without further consideration. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific and technical merit by appropriate peer review groups. The second level of review will be provided by the National Advisory General Medical Sciences Council.

##### Review criteria

- o qualifications and experience of the Principal Investigator and staff to carry out the proposed program;
- o appropriateness of the plans to develop the transition program to meet the goals of the solicitation;
- o appropriateness of the existing program, if appropriate, and of plans to modify that program;
- o availability of significant numbers of underrepresented minority students in the participating science department(s) who are interested in studying further in biomedical and health-related fields;
- o evidence of underrepresented minority students progressing to higher education in the sciences;
- o budget and cost-effectiveness of the project including appropriateness to the scope of the program, benefit to the students, number of students involved, and responsible and prudent senior personnel costs;
- o evidence of institutional commitment, for each institution, and strength of the collaborative efforts between institutions to foster professional development of underrepresented minority faculty and to train underrepresented minority students in the biomedical sciences;
- o appropriateness of the administrative plan for managing the proposed program, including adequacy of space and other institutional resources;
- o appropriateness of the system to track future course of program participants.

#### AWARD CRITERIA

The anticipated date of award is September 30, 1993. Award decisions will be based on the technical merit of the applications, the geographical distribution of the awardee institutions, and diversity of underrepresented minority student participants. Awards can be made only to institutions with financial management systems and management capabilities that are acceptable under PHS policy. Awards will be administered under the PHS Grants Policy Statement.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

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National Institute of General Medical Sciences  
Westwood Building, Room 909  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7001

Direct inquiries regarding fiscal matters to:

Ms Toni Holland  
Supervisory Grants Management Specialist  
National Institute of General Medical Sciences  
Westwood Building, Room 953  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7897

## AUTHORITY AND REGULATIONS

Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended, 42 USC 241 and 284) and administered under PHS grants policies and Federal Regulations 45 CFR Part 74 or 45 CFR Part 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## INITIATIVE FOR MINORITY STUDENTS: BRIDGES TO THE BACCALAUREATE DEGREE

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA: GM-93-002

P.T. 44, FF; K.W. 0720005, 0710030

National Institute of General Medical Sciences

Letter of Intent Receipt Date: November 20, 1992

Application Receipt Date: January 6, 1993

## PURPOSE

The National Institute of General Medical Sciences (NIGMS) and the Office for Minority Programs (OMP), National Institutes of Health (NIH), announce two initiatives directed at increasing the number of underrepresented minorities entering careers in biomedical research. The programs target two different underrepresented minority student populations: those in colleges and universities offering only Master of Science (M.S.) degree programs in biomedically-related sciences and those in two-year junior or community colleges. These have been identified as two key transition points for students considering careers in biomedical research. These initiatives seek to encourage the development of new and innovative programs and the expansion of existing programs to improve the academic competitiveness of underrepresented minority students and facilitate their transition into the next stage towards careers in biomedical research.

This Request for Applications (RFA) solicits applications for a partnership program involving two-year colleges awarding the Associate's degree and institutions awarding the Baccalaureate degree. A separate RFA (GM-93-001) describes a program targeting the transition from Master's degree granting institutions to universities awarding the Ph.D. degree.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, private and public, educational institutions and by state and local systems of higher education. Institutions that have already received NIGMS Bridge Program awards (R25) are not eligible to apply for this RFA.

An institution or system of higher education may submit ONLY ONE application for this RFA. Institutions that submit applications in response to this RFA may also apply for RFA GM-93-001; however, a separate application for each RFA is required. Institutions submitting their own applications may participate in programs with other applicant institutions so long as these interactions are consistent with institutional resources and the unified institutional plans described in BOTH applications (see Unified Plan under SPECIAL REQUIREMENTS). If an institution is involved in more than one application, justification should be provided for each.

Programs developed or modified under this initiative must be specifically designed to target underrepresented minority undergraduates majoring in the sciences. For purposes of this announcement, underrepresented minority students are individuals belonging to a particular ethnic or racial group that has been determined by the grantee institution to be underrepresented in biomedical or behavioral research. Nationally, individuals who have been found to be underrepresented in biomedical or behavioral research include, but are not limited to, Black Americans, Hispanic Americans, Native Americans and Pacific Islanders. The term "science" is used in this RFA to mean biomedical or health-related science.

Applications must include a partnership between a two-year institution that offers the Associate's degree as the only undergraduate degree in the sciences within the participating departments AND has a significant enrollment of underrepresented minorities, and a college or university offering the Baccalaureate degree in areas relevant to the biomedical sciences.

All applications must involve a partnership of at least two colleges or universities, but may involve a consortium of several institutions, and may include several institutions within a single state system. One participating institution or a single system of higher education must be designated as the grantee institution and must submit the application. The grantee institution must name the program director. Each participating institution must name one individual to act as program coordinator for that institution. Proposals must include a description of the collaborative arrangement with all participating institutions.

Institutions offering both the Associate and Baccalaureate degrees may not use funds from this program for graduates of their own Associate degree programs to enter their own Baccalaureate degree programs, even if the student is moving from one department, school, or college to another. The program seeks to promote and enhance partnerships BETWEEN institutions.

For additional requirements see SPECIAL REQUIREMENTS.

## MECHANISM OF SUPPORT

Awards under this RFA will use the institutional education project (R25) grant. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total



project period for applications submitted in response to this RFA may not exceed two years. Requested direct costs are not to exceed \$300,000 for the two-year period. Indirect costs will be paid at 8 percent of the direct costs minus appropriate exclusions. A detailed budget for each year must be provided.

This RFA is a one-time solicitation. Future unsolicited competing applications will not be accepted.

#### Allowable Costs

If appropriate, the budget request may be divided into two phases: a planning phase with its attendant budget for the development of the partnership program; and an implementation phase with its attendant budget. The planning phase costs should be minimal and not exceed a period of one year. Faculty release time for planning and implementation of the program and faculty travel related to program development may be requested.

The implementation phase may include the costs of administering and coordinating the partnership programs within and between each of the participants. Although compensation for student participation in research experiences may be requested, stipends, housing, tuition, and fees are not allowable costs under this program. However, salary/wages, tuition remission and other forms of compensation paid in lieu of wages to students performing necessary work are allowable provided there is an employer-employee relationship between the student and the institution, the total compensation is reasonable for the work performed, and it is the institution's practice to provide compensation for all students in similar circumstances, regardless of the source of support for the activity. Requests for equipment, supplies, travel, and other expenses should be limited to those necessary for program development and should be carefully and specifically justified.

#### FUNDS AVAILABLE

The funds for this program are contingent on the final level of the Fiscal Year 1993 appropriations to the Office of Minority Programs. An estimated \$7 million will be available in Fiscal Year 1993 for supporting awards made in response to RFA GM-93-001 and RFA GM-93-002. NIH staff anticipate making a combined total of 20 to 40 two-year awards for both RFAs using multi-year funding, if the NIH receives sufficient numbers of highly meritorious applications and sufficient funds for this purpose.

#### OBJECTIVES

##### Background

This program seeks to promote the initiation and development of new transitional programs, as well as the expansion and enhancement of existing programs between those institutions with departments offering only the Associate degree as the undergraduate academic degree in the sciences, which have significant enrollments of underrepresented minority students, and colleges and universities with Baccalaureate degree programs. The objective is to facilitate the transition of underrepresented minority students into Baccalaureate degree programs after obtaining the Associate's degree. Students receiving the Associate's degree in one field of science may pursue the Baccalaureate degree in a different area so long as the Baccalaureate degree is in a discipline related to the biomedical sciences.

Collaborative agreements should take the form that best fits the needs and situations of the institutions involved. The challenge for the program director, with the help of the participating partners, is to design a new partnership program, or enhance an existing program, that will focus attention and adequate resources to the Associate degree-granting institutions to enhance the academic competitiveness of their degree programs and graduates in the sciences.

##### Additional Information

These transition programs should be developed to meet the special requirements of underrepresented minority students interested in science. They may include, but are not limited to, the following elements:

- o providing laboratory research experiences at the baccalaureate institution for students enrolled in the two-year institution (students may receive compensation for these activities);
- o establishing a mentoring program with faculty at the baccalaureate institution;
- o providing research opportunities at the baccalaureate institution for faculty of the two-year college;
- o enriching the curriculum at the two-year institution (e.g., special science courses);
- o enabling students from the two-year institution to take courses and/or participate in seminar programs at the baccalaureate college;
- o developing visiting lectureships at the two-year college by science faculty from the baccalaureate institution;
- o developing courses at the two-year college jointly taught by faculty of both institutions;
- o guaranteeing acceptance as juniors into the participating baccalaureate program(s) for students who participated successfully in the enhancement program;
- o academic counseling (e.g., guidance in course selection, tracking and providing assistance to students who express an interest or show special aptitude for science);
- o additional enrichment activities, such as tutoring, to enhance the student's transition to the baccalaureate college;



- o other innovative plans to coordinate these programs.

#### SPECIAL REQUIREMENTS

Applicants should describe fully the proposed transition program and explain how its design will meet the goals of this initiative. Applicants with an existing transition program should describe that program and explain how it would be altered to meet the goals of this initiative.

#### Unified Plan

To avoid duplication of effort each institution should develop a unified plan (which may include the relevant physical, natural and/or behavioral sciences) to facilitate the transfer of its students from the Associate's degree program to the Baccalaureate degree program at another institution. Applicants should describe how this proposal fits in with the institution's overall transition plan.

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In addition, letters acknowledging participation in the program are required from each participating institution and must be signed by the program coordinator and the appropriate institutional official.

#### Reporting Requirements

A progress report will be required at the end of the planning phase (if any) or at the end of the first year, whichever is shorter. A final report will be required 90 days after the termination date of the award and must include a Statement of Appointment Form (form 2271) for each student participant as well as a report of the benefits to students of the partnership program.

#### Student Population and Career Tracking

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The applicant should describe a system by which it would monitor and track the students participating in this program, including their future careers, in order to evaluate the success of the program.

#### Other Training Programs

Colleges with any NIH funding such as the Minority Access to Research Careers (MARC), Minority Biomedical Research Support Program (MBRS), National Research Service Award (NRSA) training grants, and/or project grants, or other sources of funds such as National Science Foundation grants or Howard Hughes grants, should define the relationship between those programs and this transition program. They should delineate how this enhancement program will influence their partnerships with the other participants and the manner in which underrepresented minority students in the transition program will interact with these other sources of support.

#### LETTER OF INTENT

Prospective applicants are requested to submit, by November 20, 1992, a letter of intent that includes a descriptive title of the proposed plan, the name, address, and telephone number of the program director, the identities of other key personnel and participating institutions, and the number and title of the RFA. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIH staff to estimate the potential review workload and to avoid conflict of interest in the review.

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National Institute of General Medical Sciences  
Westwood Building, Room 909  
Bethesda, MD 20892  
Telephone: (301) 496-7001  
FAX: (301) 402-0019

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, NIH, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441; and from the NIGMS program administrator named below.

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Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies of the application must also be sent to Dr. Americo Rivera, Jr., at the address given below.

Applications must be received by January 6, 1993. Applications arriving after that date will be returned to the applicant.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be administratively reviewed by NIH staff. Incomplete and/or unresponsive applications will be returned to the applicant without further consideration. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific and technical merit by appropriate peer review groups. The second level of review will be provided by the National Advisory General Medical Sciences Council.

#### Review criteria

- o qualifications and experience of the Principal Investigator and staff to carry out the proposed program;
- o appropriateness of the plans to develop the transition program to meet the goals of the solicitation; appropriateness of the existing program, if appropriate, and of plans to modify that program;
- o availability of significant numbers of underrepresented minority students in the participating science department(s) who are interested in studying further in biomedical and health-related fields;
- o evidence of underrepresented minority students progressing to higher education in the sciences;
- o budget and cost-effectiveness of the project including appropriateness to the scope of the program, benefit to the students, number of students involved, and responsible and prudent senior personnel costs;
- o evidence of institutional commitment, for each institution, and strength of the collaborative efforts between institutions to foster professional development of underrepresented minority faculty and to train underrepresented minority students in the biomedical sciences;
- o appropriateness of the administrative plan for managing the proposed program, including adequacy of space and other institutional resources;
- o appropriateness of the system to track future course of program participants.

#### AWARD CRITERIA

The anticipated date of award is September 30, 1993. Award decisions will be based on the technical merit of the applications, the geographical distribution of the awardee institutions, and diversity of underrepresented minority student participants. Awards can be made only to institutions with financial management systems and management capabilities that are acceptable under PHS policy. Awards will be administered under the PHS Grants Policy Statement.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

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Direct inquiries regarding fiscal matters to:

Ms Toni Holland  
Supervisory Grants Management Specialist  
National Institute of General Medical Sciences  
Westwood Building, Room 953  
Bethesda, MD 20892  
Telephone: (301) 496-7897

## AUTHORITY AND REGULATIONS

Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended, 42 USC 241 and 284) and administered under PHS grants policies and Federal Regulations 45 CFR Part 74 or 45 CFR Part 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## NATIONAL RESEARCH SERVICE AWARD -- INSTITUTIONAL GRANTS

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA: HS-93-02

P.T. 44; K.W. 0730050, 0720005

Agency for Health Care Policy and Research

Application Receipt Date: January 11, 1993

### PURPOSE

The Agency for Health Care Policy and Research (AHCPR) awards National Research Service Award (NRSA) institutional grants (T32) to eligible institutions to develop or enhance research training opportunities for qualified individuals selected by the institution who have demonstrated an interest in health services research and who seek to prepare for careers in the systematic examination of the organization, provision, and financing of health care services.

The purpose of these awards is to assist domestic institutions in supporting predoctoral and postdoctoral academic training. The awards allow trainees to gain at least one year of experience in applying research methods to the evaluation of health services. The AHCPR does not support short-term training.

### AREAS OF TRAINING

AHCPR-sponsored NRSA grants emphasize multidisciplinary health services research training. This training should provide the conceptual and methodological foundation for investigating some or all of the following health care areas:

- o Primary care issues, including the development of techniques to measure the effectiveness of managing health care conditions.
- o Appropriateness and effectiveness of alternative treatments in terms of patient outcomes and use of services.
- o Factors affecting the dissemination and assimilation of information on health care technologies and other aspects of clinical practice.
- o Determinants of successful health care market reform, including incentives for efficient choices by health care purchasers and for effective management by health care providers;
- o Alternative approaches to organizing, financing, and reimbursing for health care services and their effects on cost, quality, and access.
- o Application of medical informatics to the development of expert systems for treatment selection and diagnosis.
- o Practice-based research, including clinical practice variations and guideline development.
- o Availability, accessibility, effectiveness, and quality of care for low-income groups, minorities, and the elderly.
- o Medical malpractice and liability.
- o Delivery of health services to the medically underserved, especially in rural areas.
- o Cost-effectiveness and cost-benefit analysis, including the allocation of health care resources and relationship to health status.
- o Organizational structure, resource use, and costs of care for persons with HIV-related illnesses.
- o Alternative delivery systems, providers, and practice patterns in long-term care, including home and community-based care.

### ELIGIBILITY REQUIREMENTS

#### For Institutions

Domestic non-profit private and public institutions may apply for grants to support doctoral and postdoctoral health services research training programs. The applicant institution must have the staff and facilities required for the proposed program. The training program director at the institution will be responsible for the selection and appointment of trainees and for the overall direction of the program.

Institutions may apply for support for predoctoral students, postdoctoral students, or a combination. Applicants should include a rationale for their proposed choice of supporting the level(s) of students requested. An applicant may request as many postdoctoral or predoctoral positions as the proposed program can adequately accommodate; but the number of positions awarded will be determined by the review process, program needs, and availability of funds.

#### For Trainees

Individuals to be trained must be citizens or noncitizen nationals of the United States or have been lawfully admitted for permanent residence (that is, in possession of the Alien Registration Receipt Card I-551 or I-151) at the time of appointment. Individuals on temporary or student visas are not eligible.

A postdoctoral student, as of the beginning date of the NRSA appointment, must have a Ph.D., M.D., D.O., or other doctoral degree, or an equivalent degree from any accredited domestic or foreign institution. Certification by an authorized official of the degree-granting institution that all requirements for the doctoral degree have been met is acceptable.

Predocutorial trainees must have received a baccalaureate degree as of the beginning date of the NRSA appointment and must be enrolled in a program leading to a Ph.D., Dr.P.H., or equivalent degree. Individuals working toward a medical or dental degree who wish to interrupt their studies for a year or more to engage in full-time research training before completing their degree are eligible for support.

#### MECHANISM OF SUPPORT

The mechanism of support will be the National Research Service Award institutional training grant (T32).

#### General Provisions

##### Levels and Types of Training Permitted

National Research Service Awards may not be used to support studies leading to the M.D. or other similar professional degrees, or to support residencies, that is, postgraduate training for health professionals providing health care directly to patients where the majority of their time is spent in nonresearch clinical training. However, if a specified period of full-time research training is creditable toward specialty board certification, the NRSA may support such research training if the trainee has shown a strong interest in a research career.

Trainees are required to pursue their research training on a full-time basis. Because of the close relationship between teaching and research in the academic environment, trainees are permitted, with the approval of AHCPR, to teach if it can significantly contribute to their academic training. Teaching by trainees may not take up more than 10 percent of work time during the year or exceed four hours each week.

Research trainees who are clinicians are expected to devote full time to the proposed research training. Clinical duties are limited to those which are part of the training experience. Trainees appointed to the program are expected to carry out supervised health services research with the primary objective of extending their quantitative research skills and substantive knowledge in preparation for a career in academic health services research.

Institutional training grants are a desirable mechanism for postdoctoral training of physicians and other individuals with health professional degrees whose doctoral training has usually involved limited health services research experience. For such individuals, the training may be part of a research degree program. In such cases, health professional postdoctoral trainees should agree to engage in at least two years of research training beginning at the time of appointment.

#### Duration of Support

Institutional grants are made for competitive segments of five years and are renewable; individual trainee appointments should be made in increments of 12 months. No individual trainee may receive more than five years of aggregate NRSA support at the predoctoral level and three years of aggregate NRSA support at the postdoctoral level, including any combination of support from institutional training grants and individual fellowship awards, except under certain circumstances. Any exception to this policy requires a waiver from the AHCPR.

#### Recruitment of Trainees

The primary objective of the NRSA program is to prepare qualified individuals for careers in health services research. Within the framework of the program's commitment to excellence and projected needs for investigators in particular areas of health services research, attention must be given to recruiting individuals from minority groups that are underrepresented nationally in health services research. Information on plans for the recruitment of trainees must include a description of steps to be taken for the recruitment of individuals from underrepresented minority groups. Competing continuation applications should include cumulative information on the recruitment of minority trainees and the subsequent career development of all trainees, including information about their minority status.

#### Payback Provisions

At the time of appointment, trainees must sign an agreement that they will fulfill the NRSA payback requirements. Recipients agree to engage in health services research and/or teaching for a period equal to the period of NRSA support in excess of 12 months. Once an individual has had 12 months of postbaccalaureate NRSA support, all subsequent NRSA support is subject to payback.



Recipients must undertake the obligated service on a continuous basis within two years after termination of NRSA support. Individuals who fail to fulfill their obligation through service must pay back the total amount of NRSA funds paid to them for the obligation period plus interest at a rate determined by the Secretary of the Treasury. Financial payback must be completed within three years beginning on the date the United States becomes entitled to recover such amount. Under certain conditions, the Secretary of Health and Human Services may extend the period for starting service or for repayment, permit breaks in the period of service or repayment, or otherwise waive or suspend the payback obligation of an individual.

Officials of the applicant organization responsible for recruitment of trainees should familiarize themselves with the terms of the service requirements and explain them carefully to prospective training candidates before an appointment at the institution is offered.

#### Stipends and Other Training Costs

For predoctoral trainees at all levels of experience, the stipend level (effective October 1, 1990) is \$8,800 per year.

For postdoctoral trainees, the stipend for the first year of support is determined by the number of years of relevant postdoctoral experience at the time of appointment. Relevant experience may include research experience (including industrial), teaching, internship, residency, clinical practice, or other time spent in full-time studies in a health-related field beyond that of the qualifying doctoral degree. The stipend for each additional year of NRSA support is the next level on the stipend scale. Current postdoctoral stipend levels, effective October 1, 1990, are as follows:

Years of relevant experience	Stipend
0	\$18,600
1	19,700
2	25,600
3	26,900
4	28,200
5	29,500
6	30,800
7 or more	32,300

NRSA stipends may be supplemented by an institution from non-Federal funds. Federal funds may be used for stipend supplementation only if specifically authorized under the terms of the program from which the supplemental funds are derived. An individual may make use of Federal educational loan funds or VA benefits when permitted by those programs.

Trainees may be permitted to receive compensation for work in some other position (for example, teaching or laboratory assistance) when the trainee is in an employee-employer relationship, the payments are for services rendered, and the situation otherwise meets conditions for student compensation as specified in the PHS Grants Policy Statement. Compensation may not be paid from a research grant that supports the trainee's dissertation or the same research as that of the training program. Compensation for services must occur on a limited, part-time basis apart from the normal full-time training activities that require a minimum of 40 hours per week.

Under no circumstances may the conditions of stipend supplementation or student compensation for coincidental employment detract from or prolong the research training.

The Tax Reform Act of 1986, Public Law 99-514, affects the tax liability of all individuals supported under the NRSA program. Degree candidates who, prior to the enactment of Public Law 99-514, were able to exclude all monies received under a NRSA award from their reported income, may now exclude only course tuition, fees, books, supplies, and equipment required for attendance. Nondegree candidates, who formerly were able to exclude from stipends \$300 a month for a period not to exceed three years, are now required to report all stipends and any monies paid on their behalf for course tuition and fees required for attendance. These statutory requirements became effective January 1, 1987.

The AHCPR is not in a position to advise students or institutions about their tax liability. In any event, changes in the taxability of stipends in no way alter the relationship between NRSA trainees and their institutions. NRSA stipends are not now, and never have been, salaries. Trainees supported under a National Research Service Award are not in an employer-employee relationship with the AHCPR or with the institution in which they are pursuing research training.

Tuition and fees, including medical insurance for the trainee, are allowable trainee costs if such charges are required of all persons in a similar training status at the institution, regardless of their source of support; family medical insurance is not an appropriate charge to the NRSA grant. Tuition at the postdoctoral level, if justifiable, is limited to that required for specific courses in support of the approved training program. Annual increments in tuition costs beyond the first year of a multiyear award (generally five years) may not exceed six percent.

Trainee travel, including attendance at scientific meetings, that the institution determines to be necessary to the individual's training is an allowable cost.

Institutional costs of \$1,500 per year for each predoctoral trainee and \$2,500 per year for each postdoctoral trainee may be requested to defray the cost of other training-related expenses, such as staff salaries, consultant costs, equipment, research supplies, and staff travel. Also, the institution will receive indirect costs based on eight percent of total allowable direct costs (exclusive of tuition, fees, and health insurance) or their actual indirect cost rate, whichever is less. Applications from State and local government agencies may request full indirect cost reimbursement.

## FUNDS AVAILABLE

AHCPR expects to fund approximately three to five awards in response to this RFA; the total amount available is not expected to exceed \$1,000,000.

This announcement is made subject to availability of funds. The AHCPR reserves the right to withdraw this announcement if funds do not become available.

## APPLICATION PROCEDURES

Application are to be made on grant application form PHS 398 (rev. 9/91). This revision includes special instructions for institutional NRSA research training grants. Applicants are reminded that the 25-page limit on the narrative section must be observed.

The application form is usually available at institutional offices of sponsored research or their equivalent. If forms are not available locally, send a request accompanied by a self-addressed mailing label to:

Office of Scientific Review  
Agency for Health Care Policy and Research  
2101 East Jefferson Street, Suite 602  
Rockville, MD 20852  
Telephone: (301) 227-8449

Applications must be received at the Division of Research Grants, NIH, on or before January 11, 1993. Late applications will be returned. An original and three copies of the completed application must be mailed to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Insert the title of this RFA, National Research Service Award--Institutional Grants, and the RFA number, HS-93-02, on line 2a of the application face page. The RFA label in the form PHS 398 must be affixed to the bottom of the face page of the original copy of the application. Failure to use this label could result in delayed processing of your application such that it will not reach the review committee in time for review.

Two information copies must also be sent to:

Director, Office of Scientific Review  
Agency for Health Care Policy and Research  
2101 East Jefferson Street, Suite 602  
Rockville, MD 20852

## REVIEW CONSIDERATIONS

Applications will be evaluated for merit by an AHCPR initial review group (IRG). The IRG will consider the following criteria in its review:

- o Objectives and design of the proposed training program and the probability of achieving stated goals; for renewal applications, documentation of past results in meeting goals.
- o Substantive content of the proposed program and its relevance to current health care concerns, including courses offered.
- o Qualifications and responsibilities of the program director.
- o Qualifications of the program's faculty, including ongoing health services research support.
- o Documentation of availability of qualified candidates and program's plans for recruitment and selection of trainees, including minority trainees.
- o Institutional commitment to providing a quality training environment, including availability of space and facilities, curriculum time, and research support.
- o Demonstration of cooperation by any collaborating facilities or institutions in providing experience and research training sites for trainees and mechanisms for integration of trainees.
- o Proposed methods for monitoring and evaluating performance of trainees and of the overall program. This includes tracking graduates after completion of training and record of trainees in establishing careers in health services research.
- o Record of the training program in retaining health professional postdoctoral trainees for more than 1 year of research training.
- o Reasonableness of the proposed budget, including number and levels of trainees, in relation to the research training.

Also see "Modification of Existing Review Criteria for NRSA Institutional Research Training Grants," NIH Guide for Grants and Contracts, Volume 21, Number 11, March 20, 1992.

## Minority Recruitment Plan

All applications must include a plan to recruit individuals from underrepresented minority groups. If an application is received without a plan, review may be deferred until a plan is provided. The plan to recruit minorities will be evaluated by the initial review group after the quality of the training grant application has been assessed and the priority score has been assigned. The comments of the review committee on the plan for attracting minority individuals will be presented in a note in the summary statement. For renewal applications, this note will also cover accomplishments in recruiting and retaining individuals from underrepresented minority groups during the previous award period. Funding of an application may be delayed if the plan for recruiting underrepresented minorities is considered inadequate or, in the case of competing continuation applications, if the report of efforts to recruit minorities during the previous award period is considered inadequate.

## Training in the Responsible Conduct of Research

Applications must include a description of formal or informal instruction that addresses various aspects of scientific integrity and the responsible conduct of research. Specific elements of the plan might include the breadth of topics to be covered, qualifications of the faculty to be involved, quality of the materials to be used, and the format and/or schedule of instruction. Although the exact content of the plan is left to the individual training program, it is expected that the plan will be appropriate to the training program and will demonstrate commitment of the institution in both personnel and materials. The plan to provide instruction in the responsible conduct of research will not be considered in the assignment of a priority score. However, applications that do not contain such a plan will be considered incomplete and an award will not be made until an adequate plan is provided.

## Review Schedule

The NRSA training grant receipt date and review cycle for all applications is indicated below.

Application receipt date	Initial review group meeting	Council meeting	Earliest possible start date
Jan 11, 1993	May/Jun 1993	Sep 1993	Dec 1993

## AWARD CRITERIA

After IRG review, applications will be reviewed by the National Advisory Council for Health Care Policy, Research, and Evaluation. In addition to the recommendations of the initial review group, the Council will consider the application within the overall research and training goals of AHCPR. Funding decisions will be made based on the review groups' recommendations, the need for research personnel in specified program areas, and the availability of funds.

## INQUIRIES

Program inquiries may be directed to:

DonnaRae Castillo  
NRSA Project Officer  
Agency for Health Care Policy and Research  
2101 East Jefferson Street, Suite 501  
Rockville, MD 20852  
Telephone: (301) 227-8362

Fiscal and administrative inquiries may be directed to:

Ralph Sloat, Chief  
Grants Management Branch  
Agency for Health Care Policy and Research  
2101 East Jefferson Street, Suite 601  
Rockville, MD 20852  
Telephone: (301) 227-8447

For additional information, see the document entitled "National Research Service Awards -- Guidelines for Individual Awards - Institutional Grants," NIH Guide for Grants and Contracts (special edition), Volume 13, Number 1, January 6, 1984, usually available at the applicant institution. Further information is also available in the program announcement "National Research Service Award Institutional Research Training Grants (T32)," NIH Guide for Grants and Contracts, Volume 21, Number 11, March 20, 1992.

## AUTHORITY AND REGULATIONS

NRSA institutional research training grants are made under authority of Section 487 of the Public Health Service (PHS) Act as amended (42 USC 288). Title 42 of the Code of Federal Regulations, Part 66, is applicable to this program. The program is described under Catalog of Federal Domestic Assistance No. 93.225. This program is not subject to the intergovernmental review requirements of Executive Order 12372.



## METHODOLOGICAL STUDIES TO ENHANCE DEMOGRAPHIC RESEARCH

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: HD-93-07

P.T. 34; K.W. 0413001, 0404021

National Institute of Child Health and Human Development  
National Institute on Aging

Application Receipt Date: January 19, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

### PURPOSE

The National Institute of Child Health and Human Development (NICHD) and the National Institute on Aging (NIA) invite applications for the support of basic methodological research that will enhance the collection and analysis of data to be used to answer demographic research questions. Broad areas to be supported include research that further refines theoretical constructs and develops appropriate, valid, and reliable measures of those constructs, examines characteristics of the interview situation that may affect the collection of unbiased data, and assesses the sources of bias and the impact of biased data on results. Projects may address one or more methodological issues.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Methodological Studies to Enhance Demographic Research, is related to the priority areas of family and child health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-004734-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications for R01s may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minorities and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards.

### MECHANISM OF SUPPORT

Applications in response to this RFA will be funded through the traditional individual research award (R01) program of the NIH and the FIRST (R29) awards. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for each application submitted in response to the present RFA may not exceed five years. This announcement is for a single competition, with the application receipt deadline of January 19, 1993. The average direct cost per application will be \$140,000 within a range of \$50,000 to \$200,000. For R29 applications, the budgetary conventions governing FIRST awards will apply.

### FUNDS AVAILABLE

The NICHD has set aside \$700,000 direct costs for the first year of support for the program. It is anticipated that four or five awards will be made from NICHD funds. The average direct cost per application will thus be \$140,000, within a range of \$50,000 to \$200,000.

The NIA Behavioral and Social Research Program will fund at least two grants out of special set aside funds. Aging related applications that do not exceed \$150,000 in total costs per year and are for three or fewer years will also be eligible to compete for an additional set-aside of \$1.8 million for limited size, limited duration awards. Applications will also be eligible to compete for the general pool of grant funds.

This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the NICHD and the NIA, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

### RESEARCH OBJECTIVES

As a field of research, demography has been stretching beyond traditional boundaries, attempting to address concepts that can be difficult to measure and increasingly moving into areas that are considered sensitive. Support would be provided for further conceptual development of theoretical constructs important for advancing the field of demographic research and for the development of valid and reliable measures of those constructs.

Researchers have long been concerned about the accuracy of self-reported data. This continues to be an important area of inquiry. Often, data are collected from one person regarding activities that also involve others and at times may not even involve the respondent. The validity of the data can depend on the wording of the questions, the mode of administration, the location of interview, characteristics of the interviewer and respondent, and other aspects of the interviewing process.



Obtaining the cooperation of the respondents in sample surveys has become increasingly difficult. More effort is required to obtain minimally acceptable response rates. If the survey is longitudinal, bias can be introduced through differential attrition. Research supported under this RFA could investigate means of improving response rates to sample surveys and reducing attrition in longitudinal studies.

As the areas of inquiry become more sensitive, the possibility of extraneous influences on the data collected and the challenge of developing ways to collect unbiased data become greater. Research examining bias in responses to particular topics and ways to minimize that bias is appropriate for submission to this announcement.

Despite the best efforts of researchers, the data may have inaccuracies and biases. The critical questions then become how does one assess the imprecision in the data, and how does the bias affect the results of the research. Is the bias random or systematic with respect to other relevant factors? Applications for further development of statistical methods to correct for bias could be submitted under this RFA.

#### SPECIAL REQUIREMENTS

Annual meetings will be held to foster the sharing of information, data and other experiences. Principal and co-investigators will be encouraged to attend these meetings, and funds must be included in the application budget for one two-day meeting per year in Bethesda, Maryland to discuss the research with other investigators.

#### STUDY POPULATIONS

Research may focus on U.S. or foreign populations. Researchers are encouraged to address questions relevant to men, women, and children varying in their racial and socioeconomic background.

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91) that is available in most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, Md 20892, telephone (301) 496-7441. Applications must be received by January 19, 1993.

#### REVIEW CONSIDERATIONS

The review criteria for the research projects are:

- o scientific and technical significance of proposed research;
- o appropriateness and adequacy of the research approach and methodology proposed to carry out the research;
- o qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research;
- o availability of resources necessary to perform the research;
- o appropriateness of the proposed budget and duration in relation to the proposed research.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Virginia S. Cain, Ph.D.  
Center for Population Research  
National Institute of Child Health and Human Development  
6100 Executive Boulevard, Room 8B13  
Bethesda, MD 20892  
Telephone: (301) 496-1174

or

Richard Suzman, Ph.D.  
Behavioral and Social Research Program  
National Institute on Aging  
Gateway Building, Room 2C234  
Bethesda, MD 20892  
Telephone: (301) 496-3136

Direct inquiries regarding fiscal matters to:

Melinda B. Nelson  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
6100 Executive Boulevard, Room 8A17  
Bethesda, MD 20892  
Telephone: (301) 496-5481

or

Ms. Linda Whipp  
Grants and Contracts Management Office  
National Institute on Aging  
Gateway Building, Room 2N212  
Bethesda, MD 20892  
Telephone: (301) 496-1472

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.864 and No. 93.866. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### THE REGULATION, FUNCTION AND SPECIFICITY OF PROTEINS INDUCED IN MAMMALIAN CELLS EXPOSED TO IONIZING RADIATION

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: CA-93-02

P.T. 34; K.W. 0760070, 0765015, 0760015

National Cancer Institute

Letter of Intent Receipt Date: December 10, 1992

Application Receipt Date: February 10, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Cancer Etiology of the National Cancer Institute (NCI) invites grant applications from interested investigators through the announcement of an RFA for studies of the function and regulation of expression of proteins differentially expressed in mammalian cells exposed to ionizing radiation. The focus of this initiative is the molecular description of the function and regulation of radiation-modulated proteins formed in mammalian cells in response to ionizing irradiation. The RFA will emphasize direct analysis of the genes and gene products associated with ionizing irradiation of mammalian cells.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, The Function, Regulation and Specificity of Proteins Induced in Cells Exposed to Ionizing Radiation, is related to the priority area of biomedical research. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit institutions, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA is a one-time solicitation and will be supported through the National Institutes of Health (NIH) traditional research project grant (R01). The applicant will have the sole responsibility for planning, directing and executing the proposed research. Awards will be administered under Public Health Service grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000 revised October 1, 1990. The total project period for each application submitted in response to the present RFA may not exceed four years. Competitive continuation applications will compete with all other unsolicited applications and be reviewed by a standing Division of Research Grants study section.

#### FUNDS AVAILABLE

The intent of this research initiative is to fund approximately six individual research grants, with total program costs not to exceed \$1,000,000 for the first year. This funding level will be dependent on receipt of a sufficient number of grant proposals of high scientific merit. Support for this RFA is provided for in the financial plans of the NCI. However, award of grants responding to this RFA will be contingent on the availability of funds at the time the awards are made.

#### RESEARCH OBJECTIVES

This RFA will permit a wide range of research activities, including, but not limited to, the following objectives:

- o Studies to determine the biochemical and molecular functions carried out by the uncharacterized RMPs, to relate them to poorly understood radiologic endpoints in mammalian cells such as radiation-induced arrest of the cell cycle, repair of radiation damaged DNA, radiation-induced mutagenesis, transformation, and cell survival.

- o Research to identify the radiogenic lesions that trigger the differential expression of the uncharacterized RMPs.

- o Analysis of the genetic organization of the uncharacterized RMP structural genes and the mechanisms of regulation that govern their expression.

- o Determination of the effects of radiation quality on differential expression of the uncharacterized RMPs, specifically the efficacy of high-LET radiation should be compared with low-LET radiation for inducing the uncharacterized RMPs.

#### STUDY POPULATIONS

Special instructions to applicants regarding implementation of NIH policies concerning inclusion of females and minorities in clinical research study populations are not applicable to this RFA.

#### LETTER OF INTENT

Prospective applicants are requested to submit, by December 10, 1992, a letter of intent to respond to the RFA that includes a descriptive title of the proposed research, collaborations and/or collaborative agreements, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which an application may be submitted. The letter of intent helps NCI staff to estimate the review workload and to avoid possible conflict of interest in the review. The request for a letter of intent does not bind the respondent to respond formally to the RFA, nor is it required in order to respond. The letter of intent does not enter into the review of subsequent applications.

The letter of intent is to be sent to Dr. Richard A. Pelroy at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted on PHS 398 (rev. 9/91), available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7447. The format and instructions applicable to regular research grant applications must be followed in preparing a grant in response to the RFA. The RFA label available in the application form PHS 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of a grant application, and possibly preventing it from reaching the review committee in time for review. In addition, the number and title of the RFA must be typed on line 2a of the face page of the application and YES must be checked. A signed, typewritten original grant application, including the checklist, and three signed, exact photocopies, must be mailed, in one package, to the Division of Research Grants at the address below. The photocopies must be clear and single sided.

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies of the application must also be sent to:

Referral Officer  
Division of Extramural Activities  
National Cancer Institute  
Westwood Building, Room 848  
5333 Westbard Avenue  
Bethesda, MD 20892

Applications must be received by February 10, 1993. If an application is received after that date, it will be administratively withdrawn from consideration. If the application submitted in response to this RFA is substantially similar to a grant application already submitted to the NIH for review, but has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application cannot be submitted in response to this RFA that is essentially identical to one that has already been reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique. Animal and human subject approval clearances, when applicable, should be submitted with the application to expedite the review process.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be initially reviewed by the Division of Research Grants (DRG) for completeness. Incomplete or non-responsive applications will be returned to the applicant without further consideration. Review of the responsiveness of applications to the RFA will be carried out by NCI program staff. Factors considered to be important for review will include:

- o A demonstrated knowledge of the applicable science and competence with relevant methodology.
- o The scientific merit and innovation of proposed research.

- o Adequacy of facilities and special resources relevant to the RFA.
- o Cost effectiveness of the proposal and quality of scientific collaboration.

#### INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA are encouraged and may be directed to:

Richard A. Pelroy, Ph.D.  
Radiation Effects Branch  
National Cancer Institute  
Executive Plaza North, Suite 530  
Bethesda, MD 20892  
Telephone: (301) 496-9326  
FAX: (301) 496-1224

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.393, Cancer Cause and Prevention Research. Awards are made under authorization of Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 of Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***







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# NIH GUIDE

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## For Grants and Contracts

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Building 31, Bethesda, Maryland 20892

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 38, Part II of II  
October 23, 1992

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES OF AVAILABILITY (RFPs AND RFAs)

NATIONAL COOPERATIVE DRUG DISCOVERY GROUPS FOR THE TREATMENT OF OPPORTUNISTIC INFECTIONS ASSOCIATED WITH ACQUIRED IMMUNODEFICIENCY SYNDROME

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: AI-92-15

P.T. 34; K.W. 0715008, 0760035, 0755025, 0740025, 0710035, 0765012

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 15, 1993

Application Receipt Date: March 10, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

PURPOSE

The National Institute of Allergy and Infectious Diseases (NIAID) announces availability of an RFA for funding of the National Cooperative Drug Discovery Groups for the Treatment of Opportunistic Infections Associated with Acquired Immunodeficiency Syndrome (NCDDG-OI). It is the purpose of this RFA to invite applications aimed at the discovery of new, more effective, selective, and diverse therapeutic agents to treat infections caused by *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Cryptosporidium parvum*, *Toxoplasma gondii*, *Cryptococcus neoformans*, *Pneumocystis carinii*, and *Candida albicans*. Other opportunistic pathogens associated with AIDS have been excluded from this reissuance in order to achieve programmatic balance among existing NCDDG-OI Groups.



Applications that include research projects or core components from the private sector (e.g., pharmaceutical, chemical, or biotechnological companies) are encouraged.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, National Cooperative Drug Discovery Groups for the Treatment of Opportunistic Infections Associated With Acquired Immunodeficiency Syndrome (NCDDG-OI), is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for profit and non-profit organization, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

Awards will be made as Cooperative Agreements (U01s). The Cooperative Agreement funding mechanism differs from the traditional research grant in that the Government component (NIAID) awarding the Cooperative Agreement anticipates substantial programmatic involvement during performance. The nature of NIAID staff participation is described in the RFA. However, it is the Principal Investigator who defines his/her objectives in accord with his/her interests and perceptions of approaches to the treatment of AIDS-associated opportunistic infections.

The applicant institution and the Principal Investigator will be responsible for the Group's application. Awards will be made to the applicant institution on behalf of the group as a whole and not to individual research projects within the Group. The applicant institution will provide a Central Operations Office for the Group, will be responsible for the performance of the entire Group, and will be accountable for the funds awarded. The participation of the Government through the NIAID extramural staff is intended to facilitate a concerted effort by all members of the Group by providing appropriate scientific input, by making available to the Group biological materials for testing, by accessing appropriate data bases, and by providing ancillary testing and other resources available under existing contracts. The interaction of academic and non-profit research institutions with commercial organizations and Government is strongly encouraged and is expected to favor expeditious discovery and development of agents active against OIs.

## FUNDS AVAILABLE

The NIAID anticipates making five to seven awards, based on highest program priorities, for project periods up to three years for new applications and up to four years for successful competitive renewals. The NIAID has set aside \$3.5 million total costs for first year funding. This level of support is dependent on the receipt of a sufficient number and diversity of applications of high scientific merit. Although this program is provided for in the financial plans of the NIAID, awards pursuant to this RFA are also contingent upon the availability of funds for this purpose.

It is anticipated that no more than one Group each will be funded for *M. tuberculosis*, *T. gondii*, *P. carinii*, *C. parvum*, *M. avium*, *C. neoformans*, or *C. albicans* (with restrictions) as a result of this RFA. Awards will be subject to a limit of \$650,000 in total (direct and indirect) costs for the first year with subsequent years funded at a level no greater than the first year plus 4 percent, assuming satisfactory progress has been made and reported. Applications with budgets in excess of \$650,000 total first year costs will be returned without review.

## RESEARCH OBJECTIVES

Opportunistic infections (OIs) are the major causes of morbidity and mortality in HIV disease. Available drugs to treat the OIs have limited value because of toxicity and other adverse reactions. Prolonged immunosuppression requires treatment and prophylaxis regimens that are lengthy and often expensive. There are no proven therapies effective for *C. parvum* and *M. avium* infections, and limited treatment options are available for infections caused by *T. gondii*, *M. tuberculosis*, *P. carinii*, *C. neoformans*, and *C. albicans*. The need exists for more potent and selective therapeutic agents with activity against these OIs, and particularly multidrug resistant forms of *M. tuberculosis*.

The purpose of this RFA is to encourage investigators from diverse fields and with relevant expertise to collaborate and to explore new avenues utilizing recent advances in molecular biology, biochemistry, and molecular modelling for identification of new therapeutic targets. The NCDDG-OI program provides a mechanism for a formalized collaboration between scientists from universities, pharmaceutical companies and Government, and was initiated in order to generate new approaches and strategies for drug discovery and to rapidly translate such concepts into potentially effective therapy. Results from proposed research should be used to identify and develop new potential treatments worthy of further development in clinical trials.

This RFA encourages participation by Groups proposing to study *M. tuberculosis*, *M. avium*, *C. parvum*, *T. gondii*, *C. neoformans*, *P. carinii*, or *C. albicans*. Applications focusing on drug discovery based on: (1) the molecular biology, biochemistry and metabolic activities of these organisms (excluding antifolates for *Pneumocystis* and *Toxoplasma*, and triazoles or polyenes for *C. albicans*); (2) novel drug targets; or (3) effects of host-parasite interaction are strongly encouraged. Other organisms causing infections that are also associated with AIDS have been excluded due to competing priorities and to achieve programmatic balance within the NCDDG-OI program. Scientists studying opportunistic infections associated with AIDS whose research does not lie within the areas

defined as responsive to this RFA are strongly encouraged to apply for investigator-initiated grants through the R01, R29, and R43 (Small Business Innovative Research Program) mechanisms.

#### SPECIAL REQUIREMENTS

An NCDDG-OI must be composed of a minimum of two independent laboratory research projects and may consist of scientists from a combination of academic, non-profit research, and commercial organizations. For the purpose of this RFA, two (or more) projects within a single company or academic department will not be considered independent. A core component cannot be used toward fulfillment of the requirement for two projects.

Each NCDDG-OI will be assembled by the Principal Investigator to form a multidisciplinary consortium that acts as a unit and represents the various skills needed to successfully design, synthesize, and evaluate, at the preclinical level, potential therapeutic agents useful in the treatment of opportunistic infections in AIDS patients. While it is anticipated that complete drug discovery and development of new therapies will not occur within the project period for all Groups, a rationale for the most likely utility of discoveries made within the NCDDG-OI must be included. Specifically excluded from the Group's activities are studies related to clinical evaluations.

Projects or cores with proposed animal model development must be essential to targeted drug discovery and required to attain the objectives of the Group. Testing of natural products, biologics and/or synthetic compounds must not exceed 25 percent of the total level-of-effort of the Group. Random or large scale screening of compounds will not be supported under this RFA.

Each applicant Group must provide a detailed description of the approach to be used for obtaining patent coverage for discoveries and for licensing where appropriate, in particular where the invention may involve investigators from more than one institution. In addition, each Group must provide a detailed description of the procedures to be followed for the resolution of legal problems that may develop. The NIAID will not be a partner in any patents or royalties ensuing from this research. The patent agreement, signed and dated by the organizational officials authorized to enter into patent arrangements for each Group member and member institution, must be sent before the application deadline to Dr. Barbara Laughon, at the address listed under INQUIRIES.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of Project Leaders and other key personnel and their participating institutions, the title of each project, and the number and title of the RFA.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of expected applications. It allows NIAID staff to estimate the potential workload for reviewers and to avoid possible conflict of interest in the review process. The letter of intent is to be sent to Barbara Laughon, Ph.D. (address below).

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for cooperative agreements. These forms are available at most institution sponsored research offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

Applications must be received by March 10, 1993. If an application is received after that date, it will be returned to the applicant.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants for completeness and by NIAID staff for responsiveness. Incomplete and non-responsive applications will be returned to the applicant without further consideration.

Those applications considered responsive to the RFA may be subjected to a triage review by an NIAID peer review group, before or during the review committee meeting, to determine the scientific merit relative to the other applications submitted in response to the RFA. The NIAID will withdraw from further competition those applications judged to be non-competitive for award and will notify the Principal Investigator and institutional official.

Those applications judged to be competitive will be reviewed for scientific and technical merit by an appropriate peer review committee convened by the Division of Extramural Activities, NIAID in June 1993. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council in September 1993. Award dates are anticipated to be December 1993.

## INQUIRIES

It is essential that prospective applicants obtain a copy of the RFA before preparing an application. Written and telephone requests for the RFA and the opportunity to clarify issues or questions from potential applicants are welcome. Requests for the RFA and inquiries regarding programmatic or scientific issues may be directed to:

Dr. Barbara Laughon  
Developmental Therapeutics Branch  
Basic Research and Development Program, Division of AIDS  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 2C10  
Bethesda, MD 20892  
Telephone: (301) 496-8197  
FAX: (301) 402-3211

Applicants who use express mail or courier services are advised to follow the carrier's requirements for showing a street address. The address of the Solar Building is: 6003 Executive Boulevard, Rockville, MD 20852

Inquiries regarding fiscal matters may be addressed to:

Jane Unsworth, Chief  
AIDS Grants Management Section  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B22  
Bethesda, MD 20892  
Telephone: (301) 496-7075

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.856, Microbiology and Infectious Diseases Research and 93.855, Immunology, Allergic and Immunologic Diseases Research. Awards are made under the authority of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## NATIONAL COOPERATIVE DRUG DISCOVERY GROUPS FOR THE TREATMENT OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: AI-92-16

P.T. 34; K.W. 0715008, 0755025, 0740025, 0710100

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 15, 1993

Application Receipt Date: March 17, 1993

THE REQUEST FOR APPLICATION (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The National Institute of Allergy and Infectious Diseases (NIAID) announces availability of an RFA for funding of the National Cooperative Drug Discovery Groups for the Treatment of Human Immunodeficiency Virus Infection (NCDDG-HIV). The purpose of this RFA (available upon request) is to invite applications aimed at the discovery of more effective, selective, diverse, and more risky new agents/strategies which can be used for the treatment of HIV, the etiological agent associated with Acquired Immunodeficiency Syndrome (AIDS). Applications that include research projects or core components from the private sector (pharmaceutical, biotechnologies companies) are strongly encouraged.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, National Cooperative Drug Discovery Groups for the Treatment of HIV Infections (NCDDG-HIV), is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, foreign, for-profit and non-profit, private and public organizations such as universities, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.



Awards will be made as Cooperative Agreements (U01). This funding mechanism differs from the traditional research grant in that the Government component (NIAID) awarding the Cooperative Agreement anticipates substantial programmatic involvement during performance. The nature of NIAID staff participation is described in the RFA. However, the applying Group must define its objectives in accord with its own interests and perceptions of approaches to combat HIV infection.

The applicant institution and the Principal Investigator will be responsible for the Group's application. Awards will be made to the applicant institution on behalf of the group as a whole and not to individual research projects within the Group. The applicant institution will provide a Central Operations Office for the Group, will be responsible for the performance of the entire Group, and will be accountable for the funds awarded. The participation of the Government through the NIAID extramural staff is intended to facilitate a concerted effort by members of the Group in (1) providing appropriate scientific input; (2) making available biological materials for testing; (3) accessing appropriate data bases; and (4) providing ancillary testing and other resources available under existing contracts. The interaction of academic, non-profit, and commercial organizations, and the NIAID under this Cooperative Agreement is expected to promote and expedite discoveries of new entities and strategies for the treatment of HIV infections and facilitate their subsequent development to clinical trial.

#### FUNDS AVAILABLE

The NIAID has set aside \$3.0 million for the initial year's funding of this RFA. Funding of three to four awards is anticipated. This level of support is dependent on receipt of sufficient number and diversity of applications of high scientific merit and Program relevance as stated in the RFA. Funding duration will be four years for competitive renewals and three years for new awards. Currently funded NCDDG-HIV may submit an application for competitive supplement under this RFA. All new awards are subject to a first year limit of \$800,000 in total costs (direct plus indirect costs), unless a written request for waiver is submitted, and a written approval of the request is obtained from the NIAID prior to submission of the application. Applications in excess of \$800,000 and without a written waiver from the NIAID will be returned without review. Anticipated starting date is December 1993.

#### RESEARCH OBJECTIVES

The NCDDG-HIV initiative (formerly NCDDG-AIDS), launched in 1986, is currently funding 18 Groups whose research efforts are specifically directed toward the discovery of novel agents/strategies of potential therapeutic benefit against HIV. Of the Groups currently funded, eight are eligible for recompetition in response to this RFA.

#### Research Goals and Scope:

The prime objective of this RFA is to stimulate original and innovative research of sound scientific rationale, which requires concerted Group interactions and collaborations, and that is likely to result in the discovery of new agents and modalities effective against HIV. The NCDDG-HIV program supports innovative and under-exploited studies that are at the cutting edge of biomedical research. Such studies may have a greater risk-to-benefit quotient than is currently considered under the more traditional investigator initiated (R01) mechanism, but may also have a greater potential for effective, long-term therapeutic returns. Applications by, or which include a research or a core component(s) from the private sector (pharmaceutical, biotechnological companies) are strongly encouraged, as the private sector generally has the infrastructure to continue development of a promising antiviral lead and can mobilize additional resources rapidly as needed. The salient objectives of the NCDDG-HIV program are:

- o The conceptualization, discovery and preclinical development of drugs and strategies designed to effectively treat individuals infected with HIV.
  - o The recommendation of therapies, entities or strategies for development to clinical trial.
  - o The conduct of biological, biochemical, and pharmacological studies that will permit design of predictive clinical evaluation and which may provide information leading to the future discovery of more effective treatments.
- For this RFA, research directed toward drug discovery in the following major areas will be considered responsive:
- o Discovery, development and application of modalities that inhibit HIV gene expression via interference with HIV regulatory elements.
  - o Inhibition of critical steps in HIV replication via intracellular delivery and expression of antagonists using viral vectors or other delivery strategies (gene therapy).
  - o Intervention with cellular biochemical pathways required for induction of HIV from a non-replicative state and/or for enhancement of HIV replication.
  - o Structure-based drug design and development of stable, small molecules that block HIV infection or impair virus replication.
  - o Innovative exploitation of immune properties for a targeted anti-HIV affront and immune system reconstitution.
  - o Studies of non-T cells compartment(s) that may serve in the initial infection by HIV, and which may play an essential role in virus dissemination in the body.



o New, sound conceptual strategies for the discovery of new entities or combinations for the treatment of HIV infection which are not or minimally pursued.

Prospective applicants are urged to read the RFA (available upon request, see below) for detailed description of research areas responsive, restricted and excluded under this RFA.

#### SPECIAL REQUIREMENTS

The NCDDG-HIV program will provide assistance to scientists within a Group to interact as a unit to carry out the preclinical research for discovery and development of innovative therapeutic approaches for HIV treatment. An NCDDG-HIV must be composed of a minimum of two independent laboratory research projects and may consist of scientists from academic, non-profit, and commercial research organizations. For the purpose of this RFA, two (or more) projects within a single company or academic department will not be considered independent. A core component cannot be used toward fulfillment of the requirement for two projects.

Each NCDDG-HIV will be assembled by the Principal Investigator to form a multidisciplinary consortium representing the various skills needed to successfully achieve the research objectives of the Group. A rationale for the most likely use of discoveries made by the Group must be included. Specifically excluded from the Group's activities are studies related to clinical evaluation of drugs/strategies. Projects or cores with proposed animal model development must be integrated within the major goal of targeted drug discovery and required to attain the objectives of the Group. Testing of natural products, biologics and/or synthetic compounds must not exceed 25 percent of the total level of effort of the Group. Random or large scale screening of compounds will not be supported under this RFA.

Each applicant Group must provide a detailed description of the approach to be used for obtaining patent coverage for discoveries and for licensing where appropriate, in particular where the invention may involve investigators from more than one institution. In addition, each Group must provide a detailed description of the procedures to be followed for the resolution of legal problems which may develop. The NIAID will not be a partner in any patents or royalties ensuing from this research. The patent agreement, signed and dated by the organizational officials authorized to enter into patent arrangements for each Group member and member institution, must be sent before the application deadline to:

Nava Sarver, Ph.D.  
Chief, Targeted Drug Discovery Section  
Developmental Therapeutics Branch  
Division of AIDS  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-8197  
FAX: (301) 402-3211

Applicants who use express mail or courier services should use the city and zip code of Rockville, MD 20852.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of Project Leaders and other key personnel and their participating institutions, and the number and title of this RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of expected applications. It allows NIAID staff to estimate the potential workload for reviewers and to avoid possible conflict of interest in the review process. The letter of intent is to be sent to Dr. Nava Sarver, at the above address.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying to this RFA. These forms are available at most institution sponsored research offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441. Applications must be received by March 17, 1993. If an application is received after that date, it will be returned to the applicant.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants for completeness and by the NIAID staff for responsiveness. Incomplete and non-responsive applications will be returned to the applicants without further consideration. Those applications considered responsive to the RFA may be subjected to a triage review by an NIAID peer review group, before or during the review committee meeting, to determine the scientific merit relative to the other applications submitted in response to this RFA. The NIAID will withdraw from further competition those applications judged to be non-competitive for award and will notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will be reviewed for

scientific and technical merit by an appropriate peer review committee convened by the Division of Extramural Activities, NIAID, during June 1993. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council in September 1993. The award date is anticipated to be December 1993.

#### INQUIRIES

It is essential that prospective applicants obtain a copy of the RFA before preparing an application. Written and telephone requests for the RFA and the opportunity to clarify issues or questions from potential applicants are welcome. Direct requests for the RFA and inquiries regarding programmatic or scientific issues to Dr. Nava Sarver, at the address above. Direct inquiries regarding fiscal matters to:

Ms. Jane Unsworth  
Chief, AIDS Grants Management Section  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B22  
6003 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-7075  
FAX: (301) 480-3780

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.856, Microbiology and Infectious Diseases Research and 93.855, Immunology, Allergic and Immunologic Diseases Research. Awards are made under the authority of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency Review.

#### PEDIATRIC CARDIOVASCULAR DISEASE CENTERS

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: HL-93-04-H

P.T. 04, AA; K.W. 0715040, 0755030, 0765035, 0745020, 0745027, 0745070

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: January 4, 1993  
Application Receipt Date: March 15, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The objective of this solicitation is to establish three Specialized Centers of Research (SCOR) in pediatric cardiovascular disease. The emphasis is on innovative approaches to elucidation of the etiology and pathophysiology of clinical phenomena and the translation of research findings into improved diagnosis, treatment, and prevention of cardiovascular diseases in children. Applicants are required to select a single theme and to develop interrelated research projects clearly focussed on that theme. The goal is to foster a synergistic environment for basic and clinical investigations. Applications must include both fundamental science and research involving human subjects or human material.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. The RFA, Pediatric Cardiovascular Diseases Centers, is related to the priority area of maternal and infant health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government that have established clinical programs in pediatric cardiology and the capability to conduct relevant basic research. Applications from minority individuals and women are encouraged. Foreign organizations are ineligible. International collaborations in domestic applications will only be accepted if the resources are clearly shown to be unavailable in the United States.

The Program Director must be willing to devote at least twenty-five percent effort to the SCOR and must be a project leader on at least one project or core. All other project leaders must devote at least twenty percent effort to their projects.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) specialized center grant mechanism (P50). Responsibility for planning the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years. The anticipated date of award is September 30, 1993.

## FUNDS AVAILABLE

Approximately \$3.0 million in total cost will be provided for the first year of support for the entire program. It is anticipated that three grants will be awarded under this program. However, no applicant may request more than \$750,000 in direct costs in the first year of support. Indirect costs associated with subcontracts are not included in calculations of the upper limit. Future years may be escalated at no more than four percent. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the National Heart, Lung, and Blood Institute (NHLBI), awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Administrative adjustments in project and/or amount of support may be required at the time of the award.

## RESEARCH OBJECTIVES

The goal of this program is reduction of death and disability from congenital and acquired cardiovascular diseases in children through the development of new prevention and treatment strategies. It is intended to encourage investigators with a vision of how modern technologies can be applied to the problem to propose projects that will provide insight into the etiology and pathophysiology of these diseases. For congenital heart disease, this involves new approaches to postnatal treatment and the development of methods for modifying the course of evolving cardiac malformations in the fetus. It also involves accumulating genetic information that may ultimately lead to techniques for gene therapy, although at the present time such an approach appears fraught with complexities. For acquired heart disease, this program provides the opportunity to develop knowledge regarding host factors and pathogenic mechanisms and to utilize that knowledge in prevention and treatment. Clinical investigations might be integrated with fundamental studies in a variety of ways including physiology, cell biology, genetics, molecular biology and computer technology.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review. For this RFA, the instructions should be interpreted in terms of the gender and minority status of children.

## LETTER OF INTENT

Prospective applicants are asked to submit, by January 4, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the principal investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications.

The letter of intent is to be sent to:

Chief, Centers and Special Projects Section  
Review Branch  
Division of Extramural Affairs  
National Heart, Lung and Blood Institute  
Westwood Building, Room 553A  
Bethesda, MD 20892

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

Applicants must follow carefully the instructions provided with the full RFA document in preparing their applications.

Applications must be received by March 15, 1993.

## REVIEW CONSIDERATIONS

Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NHLBI. The second level of review will be provided by the National Heart, Lung, Blood Advisory Council.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications, with added criteria evaluating the interaction between clinical and basic investigators and the overall merit of the program as a whole.



## AWARD CRITERIA

Applications must fulfill all the eligibility criteria to be considered for funding.

The most important criterion in selecting awardees will be the scientific merit as reflected in the priority score. However, factors such as program balance and available funds may enter into selection from among meritorious applications.

The anticipated date of award is September 30, 1993.

## INQUIRIES

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Constance Weinstein  
Chief, Cardiac Diseases Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3C06  
Bethesda, MD 20892  
Telephone: (301) 496-1081  
FAX: (301) 480-6282

Direct inquiries regarding fiscal and administrative matters to:

Mr. William Darby  
Grants Operation Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A11  
Bethesda, MD 20892  
Telephone: (301) 496-7536  
FAX: (301) 402-1200

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency review.

## MINORITY DISSERTATION RESEARCH GRANTS IN AGING

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: AG-93-03

P.T. 34, FF; K.W. 0710010, 0710030, 0404000, 0755030, 0785055

National Institute on Aging

Application Receipt Dates: March 18, 1993 and October 20, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW

## PURPOSE

Small grants (R03) to support doctoral dissertation research will be available for minority doctoral candidates. Grant support is designed to aid the research of new minority investigators and to encourage individuals from a variety of academic disciplines and programs to study problems in aging and issues related to aging. Specific research topics should be discussed with the National Institute on Aging (NIA). The interests of the programs are given in the full RFA.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), Minority Dissertation Research Grants in Aging, is related to the priority area of "Healthy People 2000." Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY

The applicant investigator applying for a dissertation research grant must be a minority individual enrolled in an accredited doctoral degree program in the biomedical, social, or behavioral sciences and must have approval of the dissertation proposal by a named committee. Note that this initiative is no longer limited to "underrepresented minorities". The applicant institution must be domestic and will administer the grant on



behalf of the proposed investigator. The applicant investigator for dissertation research grant support must be a citizen of the United States or hold a permanent resident visa.

#### MECHANISM OF SUPPORT

Dissertation research grants will be administered in accordance with the U.S. Code Annotated, Title 42, Part B, Section 284. Awards will depend on the availability of funds. NIA expects to fund up to 20 dissertation research projects in 1993.

Applicant investigators should request support for the amount of time necessary to complete the dissertation. However, a dissertation research grant usually is awarded for a period of 12 months but may be awarded for up to 24 months. The total direct costs of the entire project may not exceed \$25,000. A proposal that exceeds this amount will be returned. Allowable costs include the investigator's salary (not to exceed \$10,000); direct research project expenses such as travel, data processing, and supplies, and dissertation costs. No tuition or permanent equipment is allowed.

#### APPLICATION PROCEDURES

The RFA and special guidelines for dissertation grant applications must be requested from the Office of Extramural Affairs (see address below). The application is to be submitted on form PHS 398 (rev. 9/91) available from the university research office and the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7447. The special instructions described here and in the application kit must be followed. Applications will be assigned to the NIA for review and possible funding.

Applications must be received either by March 18, 1993 or October 20, 1993. Applications received after March 18, 1993 will be held for the second receipt date. Applications must be sent directly to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

The applicant must submit the original and three copies of the completed application, which includes a detailed narrative project description (not to exceed 10 pages) and letters. An additional two copies must be sent to:

Chief, Scientific Review Office  
National Institute on Aging  
Gateway Building, Suite 2C212  
Bethesda, MD 20892  
ATTN: Minority Dissertation

A letter from the faculty committee or university official directly responsible for supervising the development and progress of the dissertation research must be submitted with the application. Details of the letter are given in the full RFA.

#### REVIEW PROCESS

Dissertation research grants are competitive. Review will be conducted by a special committee convened for this purpose. Review results and funding decisions will be announced within six months after the submission date. Final funding decisions are based on the recommendations of the reviewers, the relevance of the project to NIA priorities, and the availability of funds.

#### INQUIRIES

Interested applicants must request the RFA, additional guidelines for preparing the application, and discuss the suitability of the mechanism by letter or by telephone with the person named below. The applicant will then be referred to the relevant NIA program director to discuss the suitability of the research topic.

Phyllis B. Eveleth, Ph.D.  
Deputy Associate Director and Training Officer  
Office of Extramural Affairs  
National Institute on Aging  
Gateway Building, Suite 2C218  
Bethesda, MD 20892  
Telephone: (301) 496-9322

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.366. Awards are made under authorization of the Public Health Service Act Title IV, Part A (Public Law 79-410, as amended by Public Law 99-158, 42 DSC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. The requirements of Executive Order 12372, "Intergovernmental Review of Federal Programs," are not applicable to NIA research grant programs.

NIH GUIDE, Volume 21, Number 38, October 23, 1992

RFA AVAILABLE: HL-93-15-H

P.T. 34; K.W. 0715040, 1002019, 1002058, 1002002

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: February 26, 1993  
Application Receipt Date: March 31, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The objective of this solicitation is to encourage studies leading to the application of gene targeting in rats, rabbits, and other species that are more relevant to the study of cardiovascular diseases than mice. The studies may include the development, genetic manipulation, and application of embryonic stem cells for gene targeting; the application of transgenic techniques and the development of transgenic animals; and the development and application of retroviral, antisense, ribozyme, and other approaches for producing animals of a desired genotype.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Cardiovascular Disease Genes in Animal Models, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA solicits applications for the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years. The anticipated date of award is December 1, 1993. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

#### FUNDS AVAILABLE

Approximately \$1.5 million in total costs will be provided for the first year of support for the entire program. It is anticipated that up to six grants will be awarded under this program. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the National Heart, Lung, and Blood Institute (NHLBI), awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

Hypertension, atherosclerosis, and other cardiovascular diseases are multifactorial in nature and generally involve complex interactions between genetically determined homeostatic control mechanisms and environmental factors. Research progress is greatly hampered by the lack of animal models. The best available models of hypertension, atherosclerosis, and other cardiovascular diseases are confined to rats, rabbits, and other larger animals such as pigs.

Several techniques for specifically altering the genome have been developed recently that allow single genes to be altered, ablated, or over expressed. More recently, a variety of transgenic approaches have also been developed that allow conditional gene ablation and gene inactivation by overexpression of dominant negative mutations. Application of these techniques thus provides the potential to produce animals of any desired genotype, and have resulted in major new insights into our understanding of development, cancer, immunology, and neurobiology. However, almost all of these studies have been restricted to investigations of mouse biology, since many well-characterized genetic strains of mice are available, much is known about mouse embryogenesis and its manipulation, and pluripotent embryonic stem cells (ES cells) have been isolated and cultured. The most powerful of these approaches is "gene targeting" by homologous recombination which has the potential to permit development of more precise animal models of human disease or to evaluate the contribution of candidate genes to disease pathogenesis in existing animal models.

A major technical difficulty in this approach, which largely limits its use to the study of murine biology, is the lack of availability of ES cells for species other than the mouse. Therefore, it is essential that cell lines be developed from well characterized and genetically stable strains. Other techniques for gene manipulation, including the development of transgenic animals, the direct microinjection of exogenous DNA into

tissues and zygotes, the use of retroviral vectors to incorporate newly introduced DNA into the genome, and the reinfestation of the germ line with endogenous retroviruses, have been used with some success in other species as well as the mouse. However, their application to the study of cardiovascular diseases in species other than the mouse is still very limited. Refinements of these approaches, such as the use of recently developed vectors that allow specific chromosomal locations to be targeted, should permit these strategies of gene manipulation to be applied more widely to investigate cardiovascular disorders in relevant species, and should allow new animal models that more precisely mimic human diseases to be developed.

To date, most transgenic models developed to gain insights into cardiovascular biology and disease have focused on phenotypic changes resulting from overexpression of candidate genes. Although useful information can be obtained from such models, they are complicated by the aberrant expression of genes. Gene ablation, on the other hand, potentially provides unique opportunities to study phenotypic changes resulting from the deletion of a single gene, in the absence of confounding alterations due to extratarget tissue gene expression or alterations in stoichiometry. The focus of this RFA, therefore, is on the development and application of techniques designed to produce transgenic models with phenotypic changes due to precise, endogenous genetic alterations.

This RFA is designed to encourage the development and application of gene manipulation technologies to studies in animals such as rats or rabbits that are more amenable to physiological manipulation than mice.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by February 26, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NHLBI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Charles L. Turbyfill  
Review Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 553A  
Bethesda, MD 20892

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, Westwood Building, Room 449, Bethesda, MD 20892 (telephone 301- 496-7441).

Send or deliver a signed, typewritten original of the application, including the Checklist, and three signed photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Send two additional copies of the application to Dr. Charles Turbyfill at the address listed under LETTER OF INTENT.

Applications must be received by March 31, 1993.

#### REVIEW CONSIDERATIONS

Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NHLBI. The second level of review will be provided by the National Heart, Lung, Blood Advisory Council.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications. Although multidisciplinary approaches are encouraged, it is not the intent of this announcement to solicit applications for large studies that would encompass several research projects, e.g., program projects.

#### INQUIRIES

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Michael C. Lin  
Hypertension and Kidney Diseases Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 4C10  
Bethesda, MD 20892  
Telephone: (301) 496-1857  
FAX: (301) 402-2044



Direct inquiries regarding fiscal and administrative matters to:

Ms. Jane Davis  
Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A15C  
Bethesda, MD 20892  
Telephone: (301) 496-7257  
FAX: (301) 402-1200

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### NEURAL, ENDOCRINE, IMMUNE, AND VIRAL INTERACTIONS, BEHAVIOR, AND MENTAL HEALTH

NIH GUIDE, Volume 21, Number 38, October 23, 1992

PA NUMBER: PA-93-009

P.T. 34; K.W. 1002030, 0710070, 0705030, 1002045

National Institute of Mental Health  
National Institute of Neurological Disorders and Stroke

#### PURPOSE

The National Institute of Mental Health (NIMH) and the National Institute of Neurological Disorders and Stroke (NINDS) invite research grant applications for studies of neuro-endocrine-immune interactions, neuroimmunomodulation, psychoneuroimmunology, and the effects of viral and other infectious challenges on such interactions. Applications are also invited for studies of the health and treatment implications of such interactions. The goal of this program announcement is to promote research which will advance understanding of how the brain influences, and is influenced by, the various systems that maintain homeostasis and defend/repair the body's tissues. This research will increase knowledge of the interrelationships between psychological states and physical health. Research is encouraged to improve behavioral and medical outcomes by the application of knowledge about neuro-endocrine-immune interactions.  
HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement, Neural, Endocrine, Immune, and Viral Interactions, Behavior, and Mental Health, is related to the priority areas of mental health and mental disorders, HIV infection, and immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3228).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, public and private, non-profit and for-profit organizations such as universities, colleges, hospitals, laboratories, research institutions, units of State and local governments, and eligible agencies of the Federal Government. Foreign organizations may apply for traditional research (R01) and small (R03) grants only. Women and minority investigators are encouraged to apply.

#### MECHANISMS OF SUPPORT

Applications are requested under the following mechanisms: traditional research grants (R01), First Independent Research Support and Transition (FIRST) awards (R29), small grants (R03) program projects (P01), career development awards (K-series), institutional training grants (T32), and individual fellowships (F-series).

#### RESEARCH OBJECTIVES

Proposed research can be directed at any level of biological organization from molecular to organismic. However, at whatever level studies are directed, applications must contain well-developed research plans addressing questions of clear and direct biological relevance. Specifically, proposed in vitro experiments should ideally seek mechanistic explanations for well-documented in vivo phenomena or should be carried out in conjunction with in vivo experiments. Applications solely based on the use of cell lines should be justified by inability to realize research objectives in vivo or by using primary cell or organ cultures.

Support is also provided for studies aimed at improving available methods for investigating the areas covered by this announcement. The following are examples of broad research topics that would be of interest. This list is not intended to be comprehensive, nor are the examples meant to be exclusive.

- o Mechanisms mediating functional interactions among the nervous, endocrine, and immune systems



- o Innervation of immune and endocrine organs and the functions accomplished by the innervating cell
- o Mechanisms involved in the conditioning of immune responses
- o Temporal and spatial distribution of immunocytes in brains of normal and ill individuals
- o Effects of cytokines and other products of immunocytes on neural cell function; expression and function of cytokines in the nervous system
- o Impact of immune deficiencies on function of the central nervous system and susceptibility to mental illness
- o Central neural circuitry and mechanisms of secretion of hormones which cooperate in the regulation of the immune response
- o Identification and characterization of molecules coordinating regulation of neuroendocrine and immune systems
- o Characterization of pathways of viral entry into the central nervous system and roles of neural and non-neural cells in this process
- o Roles of the blood-brain-barrier in impeding/facilitating brain-immunocyte-virus interactions
- o Mechanisms of viral neuropathogenesis; regional specificity; tropism for neural cells; replication and latency of slow-acting viruses such as HIV and other lentiviruses; effects on neuronal function and their mechanisms
- o Characterization of viral effects on psycho-neuro- endocrine-immune interactions
- o Use of transgenic, immunodeficient, and other mutant animals to investigate neuro-endocrine-immune interactions
- o Applications of novel techniques, such as in situ polymerase chain reaction and homologous recombination, to investigate immune and viral bases of mental disorders
- o Characterization of the effects of various mental states (e.g., stress and coping, sleep, intellectual activity, meditation) on endocrine and immune function and on health outcomes
- o Characterization of immune effects on psychological states and behavior

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affects them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the application must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Application submission should follow the PHS review and award schedule as published in the current version of Instructions for Grant Application Form PHS 398 (rev. 9/91).

Dates for the submission of new research applications (R01, R29, R03, P01, and K-series) and review cycles are as follows:

Receipt Dates	IRG Review	Council Review	Earliest Award Dates
Feb 1/Mar 1*	May/June	Sep/Oct	Dec 1
Jun 1/Jul 1*	Oct/Nov	Jan/Feb	Apr 1
Oct 1/Nov 1*	Feb/Mar	May/Jun	Jul 1

\*Amended research applications, supplemental applications and competing renewals are to be submitted on the latter dates.

Applications received after the above receipt dates are subject to assignment to the next review cycle or may be returned to the applicant.

Because institutional training grants (T32) and individual fellowship applications (F-series) have different deadlines and application procedures, applicants should contact program staff listed on page 8 and obtain necessary documentation pertaining to those mechanisms.

Applicants are to use the grant application form PHS 398 (rev. 9/91) for all grants except the F-series for which form PHS 416-1 (rev. 10/91) is to be used. The number and title of the program announcement, "PA-93-009: Neural, Endocrine, Immune, and Viral Interactions, Behavior, and Mental Health," must be typed in item number 2a on the face page of the PHS 398 application form.

Application kits containing the necessary forms and instructions for regular research grants may be obtained from business offices or offices of sponsored research at most universities, colleges, medical schools, and other major research facilities. If such a source is not available, the program officials listed under INQUIRIES may be contacted for the necessary application material.

The signed original and five legible copies of the completed application form PHS 398 or two copies of the form PHS 416-1 (rev. 10/91) must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

The Division of Research Grants (DRG), NIH, serves as a central point of receipt of applications for most discretionary PHS grant programs. Interest areas indicated in this announcement overlap with those of other Institutes, so applications received under this announcement will be assigned to an initial review group (IRG) in accordance with established PHS Referral Guidelines.

The IRGs, consisting primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit. Notification of the review recommendations will be sent to the applicant after the initial review. Applications will receive a second-level review by the appropriate Advisory Council whose review may be based on policy considerations as well as scientific merit. Only applications recommended for approval by the Council may be considered for funding.

#### AWARD CRITERIA

Criteria for scientific/technical merit review of applications will include the following: significance and originality, from a scientific or technical standpoint, of the goals for the proposed research; evidence of familiarity with relevant research literature; adequacy of the conceptual and theoretical framework for the research; adequacy of the methodology proposed to carry out the research; feasibility of the proposed research; qualifications and research experience of the principal investigator and other key research personnel; availability of adequate facilities, other resources, and collaborative arrangements necessary for the research; appropriateness of budget estimates for the proposed research activities; adequacy of plans to include women and minorities in study populations; and adequacy of provisions for the protection of human subjects and the welfare of animal subjects, as applicable.

Applications recommended for approval by the appropriate National Advisory Council will be considered for funding on the basis of overall scientific and technical merit of the research as determined by peer review, Institute program needs and balance, and availability of funds.

Grant funds may be used for expenses clearly related and necessary to conduct research projects, including both direct costs which can be specifically identified with the project and allowable indirect costs of the institution. Funds may not be used to establish, add a component to, or operate a treatment, rehabilitation, or prevention intervention service program. Support for research-related treatment, rehabilitation, or prevention services and programs may be requested only for costs required by the research. These costs must

be justified in terms of research objectives, methods, and designs which promise to yield generalizable knowledge and/or make a significant contribution to theoretical concepts.

Grants must be administered in accordance with the PHS Grants Policy Statement (rev. 10/90), which should be available from an office of sponsored research. Federal regulations at 42 CFR Part 52, Grants for Research Projects, and Title 45 CFR Parts 74 and 92, generic requirements concerning the administration of grants, are applicable to these awards.

Support may be requested for a period of up to five years. The small grants (R03) are for up to two years and are non-renewable. The period of individual fellowships may not exceed five years in the aggregate for pre-doctoral training and three years in the aggregate for post-doctoral training. Annual awards will be made subject to continued availability of funds and progress achieved. A competing supplemental application may be submitted during an approved period of support to expand the scope or protocol of a project during the approved period. A competing continuation (i.e., renewal) application may be submitted before the end of an approved period of support to continue a project.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Ljubisa Vitkovic, Ph.D.  
Chief, Neuroimmunology/Neurovirology Program  
Division of Neuroscience and Behavioral Science  
National Institute of Mental Health  
5600 Fishers Lane, Room 11C-05  
Rockville, MD 20857  
Telephone: (301) 443-5288  
FAX: (301) 443-4822  
BITNET: LV5@NIHCU

N. Herbert Spector, Ph.D.  
Division of Fundamental Neurosciences  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 916  
7550 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-5745  
FAX: (301) 402-1501

For further information on grants management issues, applicants may contact:

Diana Trunnell  
Assistant Chief, Grants Management Branch  
National Institute of Mental Health  
5600 Fishers Lane, Room 7C-23  
Rockville, MD 20857  
Telephone: (301) 443-3065

Mary Whitehead  
Chief, Grants Management Branch  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
Bethesda, MD 20892  
Telephone: (301) 496-9231

#### AUTHORITY AND REGULATION

This program is described in the Catalog of Federal Domestic Assistance No. 93.242 and 93.853. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 385) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SUPPLEMENTS FOR EMBRYONIC CRYOPRESERVATION OF HYPERTENSIVE RAT STRAINS

NIH GUIDE, Volume 21, Number 38, October 23, 1992

PA NUMBER: PA-93-010

P.T. 34; K.W. 0755050, 0715115, 0780005

National Heart Lung and Blood Institute

#### PURPOSE

The objective of this supplement program is to preserve embryos from phenotypically and genotypically unique rat strains used in hypertension research. Funds will be provided to investigators with active grants from the National Heart, Lung, and Blood Institute (NHLBI) so that embryos of hypertensive and normotensive control rat



strains with well-defined phenotypic and genotypic characteristics that are of value to the study of high blood pressure can be cryopreserved for future revitalization and use. Limited research may also be supported through this mechanism, but only if it clearly relates to the optimization of protocols for cryopreservation.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Supplements for Embryonic Cryopreservation of Hypertensive Rat Strains, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Supplemental applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government.

A respondent to this announcement must have an active grant from the NHLBI with at least two full years remaining at the time a supplemental award is made. Supplemental awards will be considered only for regular research project (R01) and program project (P01) grants.

## MECHANISM OF SUPPORT

Administrative supplements will be made for active R01 and P01 grants as described under ELIGIBILITY REQUIREMENTS.

## RESEARCH OBJECTIVES

### Summary

The objective of this program is to preserve phenotypically and genotypically unique rat strains used in hypertension research. This effort is necessary due to extensive genetic heterogeneity associated with many hypertensive rat strains and to the emergence of new molecular genetic technologies that will result in the availability of many new strains in the near future.

The administrative supplement program will allow unique and valuable strains to be preserved so that both existing and newly developed models of hypertension, including those derived from traditional breeding techniques as well as molecular genetic technologies, will be available to investigators for future use. The major emphasis of the initiative will be on embryonic cryopreservation of phenotypically and genotypically well-characterized hypertensive and normotensive control rat strains.

Much of the methodology and technology for cryopreservation of rat embryos has been adopted from similar work done with mouse embryos. Therefore, while a certain amount of research and technology development for rat embryo cryopreservation may be included as part of the goals of this program, the research component of the initiative will be limited to optimizing protocols for cryopreservation of embryos.

Examples of the types of research that would be supported include: maximization of the production of embryos in immature female rats and synchronization of embryo production in mature female rats via superovulation protocols; determination of the exact number of female rats needed to produce a bank of approximately 1,000 embryos per strain; optimization of procedures for the most efficient transfer of embryos to the revitalization state in situ; and establishment of methods of cryopreservation that ensure the maintenance of genetic integrity in stored embryos.

### Background

The impetus for this program comes from deliberations by the NHLBI Arteriosclerosis, Hypertension, and Lipid Metabolism Advisory Committee (AHLMAC) and two separate expert panels of scientists that were convened to evaluate the current status and need for genetically defined animal models for the study of hypertension.

The expert panels noted the lack of standardized genetic rat models of hypertension due to independent breeding and the absence of appropriate inbred controls. The panels assessed the extent to which phenotypic and genotypic variability among genetic rat models of hypertension is impeding research in the field. The panels commented that genetic heterogeneity can hamper the use of advanced molecular biological approaches, such as gene targeting, transgenic studies, and gene mapping; can compromise the scientific value of many studies; and can lead to wasteful and inefficient experiments that render inter-laboratory comparisons difficult.

It was also pointed out that preservation efforts will help inform the hypertension research community of the variety of acceptable models available for study and will enhance accessibility to unique strains. To ensure that well characterized genetic rat models are preserved, both panels recommended the banking of frozen embryos for maintaining unique rat strains.

Cryopreservation of rat embryos has been selected as the method for preserving valuable hypertensive strains because it is cheaper, more efficient, and safer than maintaining live colonies of rats. Technologies for the cryopreservation of embryos are already available for many species, and it should not be difficult to modify established procedures for cryopreservation of mouse embryos to apply to the rat.

Genetic rat models of high blood pressure and their normotensive controls provide many opportunities for studying physiological and biochemical mechanisms of blood pressure regulation. These models have helped in



the identification of numerous abnormalities in blood pressure homeostasis and have led to a clearer understanding of the normal mechanisms controlling blood pressure.

The spontaneously hypertensive rat (SHR) is among the most extensively used animal model for studying human essential hypertension because there are many similarities in the hypertensive disease process in the SHR and in human essential hypertensives. These include multiple genetic components of the disease; blood pressure that increases with age; myocardial, vascular, cerebral, and renal lesions; hemodynamic changes; greater severity of the disease in the male; and responsiveness to antihypertensive agents.

In spite of the wide use of SHRs and their Wistar-Kyoto (WKY) normotensive controls in research, recent studies indicate that genetic variability limits the utility of this model, particularly in molecular genetic studies. For example, WKY rats exhibit considerable heterogeneity when obtained from different sources. This heterogeneity is observed both in phenotype, e.g., differences in growth rates and blood pressures, and in genotype, e.g., variable DNA restriction fragment length polymorphisms. In fact, separate reports from a number of independent laboratories have provided molecular evidence of genetic heterogeneity in rats obtained commercially in the United States, England, Germany, and Japan.

Although a strong interest exists among investigators to study the contribution of specific genes to aberrations in blood pressure control, the application of genetic linkage, transgenic, or gene targeting technologies to the field of hypertension has been limited, in part due to the absence of clear evidence that animals from the colonies of different commercial vendors are phenotypically and genotypically identical. Although a relatively small number of investigators have thus far studied the genetic determinants of blood pressure variability, many important questions regarding the genetic basis of the disease remain, and for such questions to be answered, appropriately inbred rats of fixed genotype are crucial.

A system for banking specific hypertensive rat strains and appropriate normotensive controls will be of enormous utility to investigators studying hypertension, as well as other cardiovascular diseases affected by blood pressure status, such as cardiac hypertrophy, kidney failure, and stroke. Researchers currently spend considerable sums of money to produce and maintain strains of rats through conventional breeding programs and modern genetic approaches. Because a large amount of time and money are devoted to producing unique strains, methods of preserving animals other than through housing and further breeding must be considered.

Cryopreservation of embryos has a number of advantages over maintenance of live breeding colonies. This technology will reduce maintenance costs and can safeguard valuable animals produced through expensive and time-consuming molecular genetic techniques. Cryopreservation can also safeguard against damage to animal housing facilities, disease, and genetic contamination. While methodologies have been developed for the cryopreservation of embryos from several mammalian species (e.g., mice, rabbits, sheep, goats, cattle, horses, cats, and humans), it is only recently that techniques have been established for the cryopreservation of rat embryos.

Although it is still necessary to optimize superovulatory techniques to prepare female rats for fertilization and to take precautions to maintain genetic integrity when using cryopreservation, the state of knowledge is such that freezing of rat embryos can be undertaken without further significant financial investment in technology development. The immediate need for this type of repository activity has been emphasized in two reports issued by the National Research Council, both of which point to the necessity of preserving diverse animal species.

The NHLBI will maintain records of rat strains whose embryos are cryopreserved through this program and will publish and distribute a listing of such strains periodically. NHLBI staff will facilitate interaction among investigators who wish to use strains cryopreserved through this program. However, it will be the responsibility of individual investigators to establish agreements for usage and collaboration.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted on the following two application deadlines each year: March 8 and November 8, starting with March 8, 1993. Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, Westwood Building, Room 449, National Institutes of Health, Bethesda, MD 20892, telephone number 301-496-7441.

The title and number of the announcement must be typed in Section 2a on the face page of the application. The completed original supplemental application and five legible copies must be sent or delivered directly to:

Chief, Centers and Special Projects Section  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 553  
Bethesda, MD 20892

DO NOT SEND APPLICATION TO THE DIVISION OF RESEARCH GRANTS.

#### REVIEW PROCEDURES

All applications submitted in response to this Program Announcement will be reviewed for responsiveness to the objectives of this program. If the supplemental application is judged to be unresponsive, the applicant will be contacted and given the opportunity to withdraw the application for revision and resubmission at a future date.

The Review Branch, Division of Extramural Affairs, NHLBI, in consultation with program staff, will convene a panel of consultants to assist in the evaluation of the merit of the supplemental applications. The role of this peer review group will be to assess the uniqueness of the genotype and phenotype of the strain to be

cryopreserved and to evaluate overall strategies for cryopreservation, revitalization, and handling of requests for embryos. Following this initial technical review, the application will undergo a second level of review by NHLBI program staff.

#### APPLICATION GUIDELINES

The strain will need to be genotypically and phenotypically characterized in a standard manner so that uniqueness can be judged by an independent panel of consultants. The original source of the rats, as well as their breeding history, should be included along with a clear phenotypic and genotypic characterization as described below.

The overall phenotypic description of rat strains could potentially include a number of physiological and biochemical parameters. Careful documentation of arterial blood pressure is a necessity. The method of measurement (i.e., tail cuff, direct measurement with indwelling arterial catheter, anesthetized or unanesthetized, and any other specifics that could affect quantitation of blood pressure) must be described. A minimum of three separate measurements over a period of one week under identical conditions will generally be expected. Inclusion of mean arterial pressure, systolic and diastolic pressures, the standard deviation of the mean, and the range of pressures for each rat is suggested. The age and weight of the rats at the time of blood pressure determination, pertinent dietary information (e.g., protein, carbohydrate, fat, and mineral content), and gender-related differences in blood pressure should also be discussed.

Other phenotypic variables that have bearing on blood pressure regulation should be described. Careful documentation of strain-specific dysfunctions in blood vessel, renal, or neuronal function, or in the hormones and neurotransmitters known to influence arterial blood pressure, would be appropriate phenotypic information to discuss. Variations in strain responses to environmental stressors, such as salt-sensitivity or sensitivity to psychologic stressors (e.g., noises, fear, performance of tasks), should be considered for inclusion. In addition, documentation of a strain-specific propensity to develop end-organ damage, such as cerebrovascular disease, atherosclerosis, cardiac hypertrophy, or renal failure, should be addressed in detail. Lastly, well documented genetic sensitivities to known cardiovascular risk factors, such as obesity, insulin-sensitivity, and alterations of lipid metabolism, should be part of the phenotypic characterizations.

The genetic background of all strains to be considered for embryonic cryopreservation should be clearly described. To the extent possible, a complete genealogy should be provided for all strains and the nature of the genetic lesion should be documented by molecular analysis. For strains in which the genetic lesion has not been characterized at the molecular level, a thorough description of the non-molecular methods used for genotype assignment must be provided. For inbred strains, molecular evidence of genetic homogeneity should be documented by DNA fingerprint analysis and analysis of a panel of loci known to be highly polymorphic in the species of interest. Support for disease models maintained on non-inbred genetic backgrounds will be considered only if the reasons for using non-inbred lines are clearly justified.

The supplemental application should also include a well described experimental protocol to assess periodically the genetic viability of frozen rat embryos as a function of time. In particular, quality control protocols for damage to DNA should be discussed in the application.

The following budgetary requests would be appropriate for the supplement applications: salaries for key staff, which would include a cryobiologist and an individual with experience in endocrinological and surgical preparation of rats for embryo excision; limited supplies; and equipment for cryopreservation (e.g., a liquid nitrogen carboy). Additional funds may be requested for small research components related to the program. Potential applicants should discuss budgets with program staff prior to submission.

Current estimates are that approximately \$10,000 to \$20,000 in direct costs during the first year will be sufficient to undertake the activities outlined above for a single strain. It is recognized that costs will vary among laboratories. Preservation of approximately 1,000 embryos per strain will be recommended to cover a certain percentage of failed revitalizations. It is expected that supplement award recipients will recover costs for revitalization of embryos from investigators requesting rats of a particular strain. Such cost recovery would be considered program income and would be treated according to applicable PHS policies. For further information contact Ms. Jane Davis at the address listed under INQUIRIES.

#### AWARD CRITERIA

The following criteria will be considered in making funding decisions: the uniqueness of the rat strain and the quality of the cryopreservation protocols as determined through the review; the availability of funds; and program balance among the strains selected for preservation.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding scientific aspects of this program to:

Paul A. Velletri, Ph.D.  
Hypertension and Kidney Diseases Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 4C10  
Bethesda, MD 20892  
Telephone: (301) 496-1857  
FAX: (301) 402-2044

Direct inquiries regarding fiscal matters relating to this program to:

Ms. Jane Davis  
Chief, Blood Diseases and Resources Grants Management Section  
Grants Operation Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A15B  
Bethesda, MD 20892  
Telephone: (301) 496-7257  
FAX: (301) 402-1200

#### AUTHORITY AND LEGISLATION

This program is described in the Catalog of Federal Domestic Assistance No. 93.837. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernment review requirements of Executive Order 12372 or Health Systems Agency review.

#### IDENTIFICATION AND TREATMENT OF CHILDHOOD LANGUAGE IMPAIRMENT IN MULTICULTURAL POPULATIONS

NIH GUIDE, Volume 21, Number 38, October 23, 1992

PA NUMBER: PA-93-011

P.T. 34, AA; K.W. 0410001, 0507005

National Institute on Deafness and Other Communication Disorders

#### PURPOSE

Many children who are members of multicultural populations, such as African-, Asian-, and Hispanic-Americans, are often incorrectly identified as language impaired because culturally appropriate language assessment instruments are largely unavailable. In addition, those multicultural children with genuine language disorders in need of remediation may go unrecognized. The need for culturally sensitive assessment tools to evaluate the language of multicultural children has long been recognized, yet progress in this area is lacking. The National Institute on Deafness and Other Communication Disorders (NIDCD) encourages applications to develop or expand upon currently available diagnostic, as well as treatment procedures, for language-impaired children from multicultural environments.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Identification and Treatment of Childhood Language Impairment in Multicultural Populations, is related to the priority areas of diabetes and chronic disabling conditions and special population objectives. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0 or Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) (R29) Award or the Small Business Innovation Research (SBIR) (R43) Awards.

#### MECHANISM OF SUPPORT

The support mechanisms for grants in this area will be the investigator-initiated research grant (R01), the FIRST (R29) award, and the SBIR (R43) award.

#### RESEARCH OBJECTIVES

The United States has a culturally diverse population, with the rate of increase in the minority population accelerating in recent years. According to recent census figures, 23 million people over the age of five speak a language other than Standard English in the home. Almost half of these individuals reportedly do not speak English at all or do not speak it proficiently. A disproportionate number of children from these environments are identified as language impaired. Dialectal varieties of English are not considered a disorder or a pathological form of speech or language, although dialect speakers may have language disorders within the dialect. To make accurate diagnoses of language impairment, it is important to distinguish between those aspects of linguistic variation that represent a difference or diversity from those that represent a disorder.

In recent years, researchers and clinicians have questioned the validity of most speech and language assessment measures for multicultural children. Because of these children's diverse cultural, economic, and linguistic backgrounds, these procedures and instruments, by their content and design, often discriminate against children whose native language is not Standard English. Thus, high proportions of these children are incorrectly identified as language disordered and are subsequently placed into special education or communication disorders programs. Appropriate assessment of language skills and proper academic placement are critical if multicultural



children are to achieve their potential. Nonetheless, few standardized tests address the issues of cultural and linguistic diversity in their construction. In addition, most available instruments have not been standardized on children from different cultural, economic, or linguistic backgrounds. These problems make appropriate diagnosis and treatment difficult.

Examples of issues to be addressed in applications submitted in response to this PA include, but are not limited to, the following:

#### Language Impairment

- o Definition and characteristics of impaired language in specific cultures at varying ages (including phonology, syntax, semantics, pragmatics)
- o Bilingual proficiency and language disorders, including factors such as type of exposure to English, age of acquisition of English, and code switching

#### Assessment

- o Means of differentiating between language differences and disorders across cultural groups (that is, procedures for differentiating disordered language from normal language differences due to a nonstandard dialect of English, or to the acquisition of English as a second language)
- o Development of evaluative measures that are culturally fair, or modifications/adaptations of existing measures that would make them more culturally sensitive
- o Establishment of cultural norms for determining presence or absence of communication disorders
- o Development of language sampling procedures or observational techniques that are valid within specific cultures
- o Differing assessment models (e.g., natural context, questionnaire) and their validity
- o Factors that influence assessment process, such as the effect of ethnic group membership of the examiner on test scores; the test environment; examiner's fluency in the child's language

#### Treatment

- o Factors that impede efficacy of treatment in the clinical management of children from multicultural environments
- o Impact of cognitive factors, interpersonal and ecological factors, preferred learning style, and cultural systems of belief on response to treatment
- o Development of effective, innovative intervention strategies or models of service delivery, and frameworks for treatment within specific cultures
- o Factors related to effective language intervention, including effects of using only the first language, both the first and second languages, or English-only treatment; language skills of speech-language pathologist in both languages; effects of communication events within clinical setting on the level of linguistic performance

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, African-Americans, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.



For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications for R01 and FIRST (R29) awards are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. Applications for SBIR (R43) awards are to be submitted on the grant application form PHS 6246-1 (rev. 1/92) and will be accepted at the SBIR application deadlines as indicated in the application kit. These kits are available from most institutional offices of sponsored research, the NIDCD Program Administrator cited below, and the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application. FIRST (R29) award applications must include at least three sealed letters of reference attached to the face page of the original application. First (R29) award applications submitted without the required number of reference letters will be considered incomplete and will be returned to the applicant without review.

The completed original application and five legible copies of the PHS 398, or two copies of the PHS 6246-1, must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by an appropriate Initial Review Group within the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate National Advisory Council.

#### AWARD CRITERIA

Applications will compete for available funds with all other applications. The following will be considered in when funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Judith A. Cooper, Ph.D.  
Deputy Director, Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 496-5061  
FAX: (301) 402-6251

Direct inquiries regarding fiscal matters to:

Sharon Hunt  
Grants Management Officer  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-0909

This program is described in the Catalog of Federal Domestic Assistance No. 93.173. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

ERRATUM



RESEARCH INFRASTRUCTURE SUPPORT PROGRAM

NIH GUIDE, Volume 21, Number 35, October 2, 1992

PA AVAILABLE: PA-93-003

P.T. 14; K.W. 0715129, 0785035, 0710030

National Institute of Mental Health

The Review Criteria published for Program Announcement PA-93-003 in the NIH Guide for Grants and Contracts, Vol. 21, No. 35, October 2, 1992, were incorrect. The Review Criteria section should read as follows:

- o Significance and public health relevance of the clinical focus of the application.
- o Appropriateness and relevance of the proposed development plan; potential of the RISP plan for effecting significant and lasting improvements in the institution's capacity to conduct fundable research.
- o Likelihood that the RISP improvement effort will provide sufficient enhancement to mental health research projects so that they may become competitive for extramural funding.
- o Nature, amount, and duration of the non-Federal commitment to the project.
- o Capability of the Principal Investigator and other senior staff to provide leadership in the effort to enhance the institution's research capacity.
- o Adequate representation of minorities and women.
- o Appropriateness of the budget.
- o Adequacy of proposed procedures for protecting human and animal subjects.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 39, Part I of II  
October 30, 1992

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

### NOTICES

NOTICE TO APPLICANTS RESPONDING TO RFA DE-92-02: RESEARCH CENTERS ON ORAL HEALTH IN AGING OR RFA DE-92-03: PERIODONTAL DISEASES RESEARCH CENTERS . . . . .  
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National Institute of Allergy and Infectious Diseases  
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GENE THERAPY APPROACHES FOR CYSTIC FIBROSIS AND OTHER HEART, LUNG, AND BLOOD DISEASES (RFA HL-93-08-L) . . .  
National Heart, Lung, and Blood Institute  
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National Institute of Diabetes and Digestive and Kidney Diseases  
Cystic Fibrosis Foundation  
INDEX: DIABETES, DIGESTIVE, KIDNEY DISEASES

### ONGOING PROGRAM ANNOUNCEMENTS

NOVEL DRUG DELIVERY SYSTEMS FOR TREATMENT OF DRUG ABUSE (PA-93-012) . . . . .  
National Institute on Drug Abuse  
INDEX: DRUG ABUSE

*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

### NOTICES

NOTICE TO APPLICANTS RESPONDING TO RFA DE-92-02: RESEARCH CENTERS ON ORAL HEALTH IN AGING OR RFA DE-92-03: PERIODONTAL DISEASES RESEARCH CENTERS

NIH GUIDE, Volume 21, Number 39, October 30, 1992

P.T. 04; K.W. 0710010, 0715148, 1014006

National Institute of Dental Research  
National Institute on Aging

In the past, it has been common practice for applicants responding to Requests for Applications (RFA) issued by the National Institute of Dental Research (NIDR) or the National Institute on Aging (NIA) for specialized research centers grants (P50) to amend unfunded applications and submit them as unsolicited program project grant (P01) applications. Alternatively, subprojects from unfunded P50 grant applications have been amended and submitted as applications for other support mechanisms such as research project grants (R01) or small grants (R03). The NIDR accepts both R01 and R03 applications; the NIA does not accept R03s.

Applicants responding to RFA DE-92-02, Research Centers on Oral Health in Aging (NIH GUIDE, Vol. 21, No. 10, March 13, 1992) or RFA DE-92-03, Periodontal Diseases Research Centers (NIH GUIDE, Vol. 21, No. 12, March 27, 1992) should be aware that, because of fiscal constraints, it is unlikely that the NIDR or the NIA will be able to fund P01 grant applications resulting from the amendment of unfunded P50 applications submitted in response to RFA DE-92-02 or RFA DE-92-03. Submission of program project applications with goals similar to those



included in either of these RFAs is discouraged. However, applicants are encouraged to amend promising subprojects from unfunded P50 applications and apply for support under other grant mechanisms.

#### INQUIRIES

Inquiries concerning this policy may be addressed to:

Director, Extramural Program  
National Institute of Dental Research  
Westwood Building, Room 503  
Bethesda, MD 20892-4500  
Telephone: (301) 496-7723

Associate Director for Extramural Affairs  
National Institute on Aging  
Gateway Building, Room 2C218  
Bethesda, MD 20892-4500  
Telephone: (301) 496-9322

#### AMENDMENT TO CURRENT PROGRAM ANNOUNCEMENT NUMBER PA-91-38

NIH GUIDE, Volume 21, Number 39, October 30, 1992

P.T. 34; K.W. 0715095, 0715129, 0715177, 0414004

National Institute of Mental Health

The National Institute of Mental Health announces a change in the research and training support for the Clinical Mental Health Academic Award (K07). The current program announcement is PA-91-38. The direct cost allowance for research support and career development costs has been increased (effective October 1, 1992) from \$30,000 to \$50,000 per year.

#### INQUIRIES

Copies of the complete announcement may be obtained from:

Division of Extramural Activities  
National Institute of Mental Health  
5600 Fishers Lane, Room 9-97  
Rockville, MD 20857  
Telephone: (301) 443-4673

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### PEDIATRIC AIDS CLINICAL TRIALS PROGRAM

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: AI-92-10

P.T. 34, AA; K.W. 0715008, 0770005, 0755015

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: November 13, 1992  
Preapplication Meeting Date: December 7, 1992  
Application Receipt Date: January 21, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The purpose of this RFA is to recompet the Pediatric AIDS Clinical Trials Program in order to further stimulate pediatric AIDS research. This program, initiated in 1988, is supported by the Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID). The program is designed to provide a distinct scientific emphasis on Human Immunodeficiency Virus (HIV) disease in children and a focus for addressing therapeutic research issues related to this population.

The RFA calls for an emphasis on the development and evaluation of pediatric therapeutic research in three major areas, namely: (1) interruption of perinatal transmission of HIV, (2) antiretroviral therapy, and (3) therapy and prophylaxis against opportunistic infection in HIV disease. The target populations include: infants (0 to 12 months of age), children (13 months to 12 years of age), and adolescents (13 through 18 years of age).

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of Healthy People 2000, a PHS-led national activity for setting priority areas. This RFA, Pediatric AIDS Clinical Trial Program, is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Existing pediatric AIDS Clinical Trial Units (ACTUs), pediatric components of adult ACTUs, as well as new applicants are invited to apply.

#### MECHANISM OF SUPPORT

Awards funded under this RFA will be supported through National Institutes of Health (NIH) cooperative agreements (U01). Assistance provided through the cooperative agreement differs from the traditional research grant in that the government component (NIAID) anticipates substantial programmatic involvement during the performance of the award. All policies and requirements that govern the grant program of the PHS and the NIH apply to these cooperative agreements.

This RFA is a one-time solicitation with a specified deadline for receipt of applications. Reissuance of this initiative is uncertain. If, by the end of the third year of award, NIAID has not announced an intention to reissue the RFA, awardees who plan to apply for continuing support should contact NIAID program officials for advice on how to recompute.

#### FUNDS AVAILABLE

Approximately \$23,000,000, total costs, will be available for the first year funding. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit and availability of funds. Approximately 10-14 pediatric ACTUs will be funded under this RFA. Awards will be made for a total project period of four years. The anticipated earliest award date is September 1, 1993.

Funding beyond the first and subsequent years of the award will be contingent upon satisfactory performance during the preceding years, including meeting research objectives and patient accrual targets, and the continuing availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The primary research objectives of this Program are to evaluate the pharmacokinetics, safety, tolerance, and efficacy of agents in order to:

- o reduce the rate of perinatal transmission of HIV;
- o develop effective antiretroviral treatment of primary HIV infection; and
- o develop effective treatment and prophylaxis of opportunistic infections.

These research aims will be addressed through a multi-center clinical trials network in which Principal Investigators work collectively (as a group) and cooperatively with NIAID staff to devise and implement the most appropriate studies for these objectives.

#### SPECIAL REQUIREMENTS

##### Terms and Conditions of Award

Awardees must conduct clinical trials that focus on the three research areas listed above. At least 25 new patients per year must be accrued onto pediatric protocols. The majority of the pediatric protocols include patients to ages 17 or 18. Included may be individuals classified as adolescents. Since most current and future pediatric research protocols require multiple neurodevelopmental tests, awardees must also perform neuropsychological and neurological testing as clinical endpoints of required studies.

In addition to the 25 patients mentioned above, awardees who have a particular interest in unique aspects of research on adolescents will implement specific studies designed to focus on this population. Institutions with a special interest in neurological and neuropsychological testing will conduct studies of new and efficient methods that could be used as measures of effectiveness in clinical trials of antivirals.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by November 13, 1992, a letter of intent that includes a descriptive title of the overall proposed research, the name and institution of the Principal Investigator, and a brief description of the research proposed for each component in which participation is planned. Names of prospective co-investigators and other key personnel should be included.

A letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application. The letter of intent is to be sent to Ms. Tina Johnson at the address listed under INQUIRIES.

## APPLICATION PROCEDURES

The application will contain the following component parts:

A, B, and C. Applicants are REQUIRED to apply for: PART A, the Pediatric AIDS Clinical Trials Unit (focusing on interruption of perinatal transmission of HIV, antiretroviral therapy, and therapy and prophylaxis against opportunistic infection in HIV disease) and PART B.1, Laboratory Support. PART B.2 and B.3, Laboratory Support, and PART C, Developmental Research, are OPTIONAL.

### Organization of the Application

All applications are to be submitted on the form PHS 398 (rev.9/91). The application must be assembled and paginated as one complete document. A separate narrative and itemized budget with justifications must be prepared for each component for which support is being requested.

### Budget Requirements

#### PART A - CLINICAL BASE BUDGET

That portion of the Pediatric ACTU budget specifically related to patient care is called the Clinical Base Budget. It will include the resources required to accrue a projected number of new patients on an annual basis.

Clinical budgets will be constructed by relating the cost of performing a protocol (protocol specific and non-specific costs) to the projected number of patients to be accrued. These costs will represent the major portion of the clinical base budget.

#### PART B - LABORATORY SUPPORT BUDGET

A detailed budget for the first year and for all four years of support must be prepared for each laboratory component for which you are applying. It is anticipated that Laboratory Support awards will not exceed \$200,000 direct costs per year per laboratory.

#### PART C - DEVELOPMENTAL RESEARCH BUDGET

As with Part B above, a detailed 12-month budget and a summary four-year budget must be prepared for each developmental research project proposed, following the instructions in Form PHS 398. It is anticipated that developmental research awards (Part C) will not exceed \$100,000 direct costs annually per application. Applicants may apply for more than one optional component.

Each project under Laboratory Support and Developmental Research components will be REVIEWED INDEPENDENTLY and should contain sufficient information and detail to assure a thorough review.

In order to provide a forum during which prospective applicants may obtain additional information, further clarification and assistance, a Preapplication Meeting will be held on December 7, 1992 in Bethesda, MD. You may contact Ms. Tina Johnson at the address listed under LETTER OF INTENT after November 6, 1992 to obtain specific information about the meetings.

The deadline for receipt of applications is January 21, 1993. Applications received after this date will be considered as nonresponsive to this RFA and returned without review.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by DRG staff for completeness and by NIAID staff for responsiveness. Incomplete applications will be returned to the applicant without further consideration.

Those applications that are complete and responsive will be evaluated in accordance with the criteria stated in the RFA for scientific/technical merit by an appropriate peer review group convened by the NIAID. Those applications may be subjected to triage by a Special Review Committee (SRC) to determine their scientific merit relative to other applications received in response to this RFA. The NIH will administratively withdraw from competition those applications judged to be noncompetitive and notify the applicants and the institutional business officials. Those applications judged to be competitive will undergo further evaluation for scientific merit by a Special Review Committee consisting primarily of non-Federal scientific experts. Members of the committee that conducted the triage will also serve on this committee. The second level review will be provided by the National Advisory Allergy and Infectious Diseases Council.

### Laboratory Support and Developmental Research

Applications for Laboratory Support and Developmental Research will be evaluated independently from the evaluation of Part A.

Applications for Laboratory Support and Developmental Research that are complete and responsive may also be subjected to a triage by a peer review group to determine their scientific merit relative to other applications received in response to each component in this portion of the RFA. This procedure follows exactly the discussion in the preceding paragraph.

#### INQUIRIES

Written and telephone inquiries concerning the RFA are encouraged. The following NIAID staff will be available to answer questions regarding the preparation of the application in response to the RFA.

Direct inquiries concerning the programmatic aspects of this RFA to:

Tina Johnson, M.A.  
Clinical Research Management Branch  
Division of AIDS  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 2A09  
Bethesda, MD 20892  
Telephone: (301) 496-8214

Direct inquiries regarding budget issues to:

Ms. Mary Kirker  
Deputy Chief, Grants Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B22  
Bethesda, MD 20892  
Telephone: (301) 496-7075

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.856, Microbiology and Infectious Diseases Research and 93.855, Allergy, Immunology and Transplantation Research. Cooperative agreements are awarded under the authority of the Public Health Service Act, Title IV, Section 301 as amended, Public Law 78-410; Public Law 97- 219; Public Law 99-500; and Report 99-711 to accompany HR 5233 and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12371 or Health Systems Agency review.

#### AIDS CLINICAL TRIALS UNITS AT MINORITY INSTITUTIONS

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: AI-92-14

P.T. 34, FF; K.W. 0715008, 0755015, 0745070

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: November 16, 1992

Application Receipt Date: January 21, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

#### PURPOSE

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for AIDS Clinical Trials Units (ACTUs) at Minority Institutions. The purpose of this RFA is to solicit applications from minority institutions to establish adult ACTUs and to become part of the AIDS Clinical Trials Group (ACTG).

Institutions that have more than 50 percent minority student enrollment and award the M.D., D.D.S., D.V.M., or other doctoral degree in the health professions are encouraged to apply.

The ACTG is a network of 35 domestic biomedical research institutions that, in aggregate, has the capabilities to develop new therapeutic interventions from initial clinical trials in human subjects to their final approval by the Food and Drug Administration. The ACTG evaluates the safety and efficacy of therapeutic interventions for the treatment of Human Immunodeficiency Virus (HIV) infection, associated opportunistic infections and malignancies, and neurological complications of AIDS.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, AIDS Clinical Trials Units at Minority Institutions, is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).



#### ELIGIBILITY REQUIREMENTS

This competition is limited to domestic universities or colleges that possess the capabilities to conduct clinical research on HIV infection and AIDS. Applications may not contain an international component. Preference will be given to institutions that have more than 50% minority student enrollment.

#### MECHANISM OF SUPPORT

Awards will be made as Cooperative Agreements (U01). The Cooperative Agreement funding mechanism differs from the traditional research grant in that the Government awarding component (NIAID) anticipates substantial programmatic involvement during the performance of the project. However, applicants must define their own objectives in accord with individual interests and approaches to conducting the research. There is no intent, real or implied, to limit the freedom of the investigators. All policies and requirements that govern the grant program of the U.S. Public Health Service and the National Institutes of Health apply to these Cooperative Agreements. The total project period for applications submitted in response to this RFA will not exceed four years. The anticipated award date is September 1, 1993. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also.

#### FUNDS AVAILABLE

The NIAID anticipates that \$3,800,000 will be available in the initial year for funding applications in response to this RFA. The award of grants pursuant to this RFA is contingent on the continuing availability of funds for this purpose and on the receipt of a sufficient number of applications of high scientific merit. It is anticipated that three to four applications will be funded under this RFA.

#### RESEARCH OBJECTIVES

It is the intent of this competition to enhance the research capabilities of the ACTG by establishing clinical trials units at minority institutions. With a disproportionate number of minorities infected with HIV relative to the overall population, it is of high priority to encourage participation by these individuals in AIDS clinical trials. Minority institutions are in a unique position to access and serve this patient population. The research objectives will be accomplished through the development of protocols, accrual of patients to ACTG protocols, and the publication and presentation of data. The research agenda and priorities will be established by the Executive Committee of the ACTG and the NIAID. Scientific areas of priority include interventions for the treatment of HIV infection and for the treatment and prophylaxis of opportunistic infections associated with HIV infection. Studies of HIV-associated malignancies and neurological complications are also being encouraged. Applicants for the AIDS Clinical Trials Units also may apply for optional laboratory components in pharmacology, virology, immunology and other areas that are clinically relevant to HIV infection.

#### SPECIAL REQUIREMENTS

All awardees must be capable of enrolling a MINIMUM of 60 new patients annually on to ACTG clinical protocols for each year of the award. The investigators of the cooperative group will be responsible for the overall conduct of the research, including the development of concept sheets and protocols, accrual to protocols, production of high quality data and the timely reporting of research results. Investigator will be required to submit their data to ACTG database; however, the data will remain the property of the awardee from which they originated. The NIAID will have access to all data generated under this cooperative agreement for the preparation of internal reports and to fulfill its regulatory role as the sponsor of investigational new drugs.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR THE INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included or adequately represented in the study populations for clinical studies, a specific justification for this exclusion must be provided. Application without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by November 16, 1992, a letter of intent, that includes the name and address of the Principal Investigator, other key personnel, and participating institutions. The letter of intent is requested to provide an indication of the number and scope of applications to be received and to promote early interaction between NIAID staff and the applicant. The letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application. Letters of intent are to be sent to Frederick Batzold, Ph.D., at the address listed under INQUIRES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev.9/91) is to be used in applying. These form are available at most institutional offices of sponsored research and from the Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7447. The application receipt date is January 21, 1993. Applications received after this receipt date or those that are incomplete or nonresponsive to this RFA will be returned to the applicant without review. Submit a signed, typewritten original of the application and three exact, single-sided photocopies (including Appendices) in one package to:

Division of Research Grants  
National Institute of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Submit two additional exact, single-sided photocopies of the application including Appendices in one package directly to:

Dianne Tingley, Ph.D.  
AIDS RRS/SRB  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C16  
6003 Executive Boulevard  
Bethesda, MD 20892

#### INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome.

Direct requests for the RFA, Letter of Intent, and inquires regarding programmatic issues to:

Frederick Batzold, Ph.D.  
Division of AIDS  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-8214  
FAX: (301) 480-5703

Direct inquiries regarding fiscal matter to:

Ms. Mary Kirker  
Grants Management Branch  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-7075

Applicants who to use express mail or courier service should substitute Rockville, MD 20852 for city, state, and zip code.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.856 and No. 93.855. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency Review.

#### COLLABORATIVE PROJECTS ON MINORITY HEALTH

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: HL-93-01

P.T. 34, FF; K.W. 0715032, 0715040, 0715165, 0745020, 0745027, 0785035

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: February 12, 1993

Application Receipt Date: March 19, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) invites the concurrent submission of small groups of scientifically related research grant applications (ROIs) with a common theme related to minority health issues and within the purview of the NHLBI. The goal of this program is to foster collaborative clinical research that focuses on new and improved approaches for diagnosis, management, and prevention of cardiovascular, lung, and blood diseases in minorities. Applicants are expected to have demonstrated expertise in the recruitment and retention of minority study participants. This solicitation is part of the NHLBI commitment to improve the health status of the American population.

The special feature of this program is the concurrent submission of research grant applications by investigators who wish to collaborate on a common theme related to clinical research on minority health issues, but do not require extensive shared physical resources or core functions to conduct their research. In order to be responsive to this RFA, a minimum of three independent investigators with related research objectives should submit concurrent, collaborative, cross-referenced individual research grant applications that address a common theme. The common theme may be one that spans the traditional boundaries of cardiovascular, lung, and blood research (e.g., thromboembolic events), or it may deal with a single disease or condition (e.g., asthma) from several points of view. Investigators may submit applications for small clinical studies, including

biobehavioral and prevention research. Applications will be reviewed for scientific merit, relevance of projects to the chosen theme, and overall proposed collaboration. Special consideration will be given to applications from minority investigators and institutions.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priorities. This RFA, Collaborative Projects on Minority Health, is related to the priority areas of cardiovascular, lung, and blood diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by all domestic for-profit and non-profit institutions, public and private, such as universities, colleges, hospitals, and laboratories.

This RFA is intended to support individual research grants for studies of minority human subjects. Therefore, basic research investigations and studies in non-minorities will not be responsive to this RFA. Large population-based studies, such as epidemiologic surveys or clinical trials, will be considered unresponsive to this announcement. Awards will not be made to foreign institutions.

## MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional individual research grant (R01). Applicants are requested to furnish estimates of the time required to achieve the objectives of the proposed research project. Up to five years of support may be requested. At the end of the official award period, renewal applications may be submitted for peer review and competition for support through the regular grant process of the NIH. It is anticipated that support for the present program will begin in September 1993. Administrative adjustments in project period and/or amount of support may be required at the time of the award. All current policies and requirements that govern the research grant programs of the NIH will apply to grants awarded in connection with this RFA.

Since a variety of approaches would represent valid responses to this announcement, a range of costs is expected among individual grants awarded. However, a collaborative group must not exceed \$1,000,000 total requested costs (direct and indirect) each year, and the average total requested cost of applications within a group must not exceed the average total cost of NHLBI R01 grants (\$220,000). Any equipment requested must be especially justified. Requests for expensive pieces of equipment are not encouraged. Collaborative arrangements involving other institutions are encouraged and should be discussed with the NHLBI program staff prior to submission of the applications.

## FUNDS AVAILABLE

Although the total costs of this program are estimated at \$5,000,000, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that four to six collaborative groups (12-24 R01 awards) will be supported under this program. The number and specific amount to be awarded will depend on the merit and scope of the applications received and on the availability of funds.

## RESEARCH OBJECTIVES

The objective of the NHLBI Collaborative Projects on Minority Health is to foster collaborative clinical research that focuses on new and improved approaches for diagnosis, management, and prevention of cardiovascular, lung, and blood diseases in minorities.

Examples of research that would be responsive to this RFA are given below. These research topics are intended to provide a perspective on the scope of research that would meet the objective of this program. It is not required that all or any of them be included in a particular group of applications. Investigators are encouraged to consider other topics relevant to this program.

- o Identification of factors responsible for variability in the clinical presentation, diagnosis, and effectiveness of treatment of cardiovascular diseases.
- o Investigation of approaches to reduce the prevalence of obesity, identify mechanism(s) by which obesity alters blood pressure, and enhance cardiopulmonary fitness, particularly among individuals at high risk.
- o Development and evaluation of programs that incorporate strategies for increasing compliance and for long-term maintenance of behavioral changes.
- o Development of age-appropriate management strategies, including methods of self-management, for the control of asthma.
- o Delineation of the etiologic and pathophysiologic factors that contribute to the increased incidence, severity, and chronicity of sarcoidosis, particularly for those individuals at high risk, and development of rational intervention strategies for its treatment.
- o Development of refinement of approaches to prevent initiation of smoking and to facilitate smoking cessation.
- o Elucidation of the mechanisms of expression and progression of tuberculosis, characterization of the natural history of HIV-associated pulmonary tuberculosis, and development of specific treatment modalities.



o Study of sickle cell disease, including development of therapies to prevent osteonecrosis of the femoral head, pulmonary lesions that cause the acute chest syndrome, strokes in young patients, and occult progressive renal lesions.

o Investigation of normal and abnormal coagulation; development of noninvasive or minimally invasive technology to evaluate the possibility of dysfunctional endothelium in sickle cell disease, particularly in those individuals with stroke.

o Development of methods and approaches to encourage blood and bone marrow donation; development of preventive and therapeutic strategies for alloimmunization.

o Development of health education and prevention programs, appropriate to particular groups, that will facilitate adoption of optimal health behaviors.

#### SPECIAL REQUIREMENTS

Upon initiation of the program, annual meetings will be sponsored to encourage an exchange of information and ideas among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a two-day meeting each year to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women and minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by February 12, 1993, a one-page letter of intent that includes identification of any other participating investigators and institutions, together with a descriptive title. The NHLBI requests such letters only for the purpose of providing an indication of the number and scope of applications to be received and, therefore, usually does not acknowledge their receipt. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter of intent is to be sent to:

Chief, Centers and Special Projects Review Section  
Review Branch/Division of Extramural Affairs  
National Heart, Lung, and Blood Institute, NIH  
Westwood Building, Room 553  
Bethesda, MD 20892

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. This form is available in the applicant institution's office of sponsored research or business office. It can also be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7447. Applicants may contact one of the program administrators listed under INQUIRIES to seek clarification or discuss any questions related to this announcement.

Applications must be received by March 19, 1993. An application not received by this date will be considered ineligible.

#### REVIEW CONSIDERATIONS

##### Review Method

Upon receipt, applications will be reviewed for completeness by the DRG. Applications will be reviewed for their responsiveness to the objective of this RFA. If an application or group of applications is judged incomplete or unresponsive, the application will be returned. If the application submitted in response to this RFA is substantially similar to a grant application already submitted to the NIH for review, but has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application cannot be submitted in response to this RFA that is essentially identical to one that has already been reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

Applications judged to be responsive will be reviewed for scientific and technical merit by an initial review group that will be convened by the Division of Extramural Affairs, NHLBI, solely to review these applications.

This initial review will include a triage; the NHLBI will withdraw from further consideration applications judged to be noncompetitive and will promptly notify the principal investigator and the official signing for the applicant organization. Those applications judged to be competitive will be further evaluated for scientific and technical merit by usual peer review procedures. Each application will receive a priority score



based upon review criteria listed below. The second level of review will be provided by the National Heart, Lung, and Blood Advisory Council.

#### Review Criteria

Factors to be considered in the evaluation of each application will be similar to those used in review of traditional research grant applications and, in addition, will include overall proposed collaboration. Major factors to be considered in the evaluation of applications will include:

- o Scientific merit of the proposed projects, including innovation, originality, and feasibility of the approach; adequacy of the experimental design and the plans for recruitment and retention of research subjects.
- o Competence of the investigators to accomplish the proposed research goals, their commitment, and the time they will devote to the program.
- o Integration of the component R01s into a coherent enterprise with adequate plans for collaboration, interaction, and communication of information among participating investigators.
- o Adequacy of facilities for performance of the proposed research including clinical facilities, proposed instrumentation and, when needed, data management systems.
- o Appropriateness of the budget for the proposed project.

#### AWARD CRITERIA

It is anticipated that four to six collaborative groups (12-24 R01 awards) will be supported under this program. The number and specific amount to be awarded will depend on the merit and scope of the applications received and on the availability of funds. Special consideration will be given to applications from minority investigators and institutions.

#### INQUIRIES

Inquiries regarding this RFA may be directed to the following program administrators:

Patrice Desvigne-Nickens, M.D.  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3C06  
Bethesda, MD 20892  
Telephone: (301) 496-1081  
FAX: (301) 480-6282

For fiscal and administrative matters, contact:

Marie A. Willett  
Grants Operation Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A12  
Bethesda, MD 20892  
Telephone: (301) 496-7255  
Fax: (301) 402-1200

#### AUTHORITY AND REGULATIONS

These programs are described in the Catalog of Federal Domestic Assistance Nos. 93.837, 93.838, and 93.839. Awards will be made under the authority of the Public Health Service (PHS) Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency Review.

# EXPLORATORY NEONATAL BRAIN DISORDERS RESEARCH GRANTS

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: NS-93-001

P.T. 34; K.W. 0705010, 0403020, 0715138, 0715027, 0710030, 0745020

National Institute of Neurological Disorders and Stroke

Letter of Intent Receipt Date: January 15, 1993

Application Receipt Date: April 8, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The National Institute of Neurological Disorders and Stroke (NINDS) announces an RFA for exploratory grant applications for the development of research centers on neonatal brain disorders. The NINDS invites initiatives directed towards the planning of new or expansion of existing resources to explore various approaches to studying the newborn at risk for brain injury. These initiatives should be well-focused and integrate multidisciplinary research capacities, encouraging combined basic and clinical research, to advance the understanding of fetal and neonatal neurological integrity and vulnerability to brain injury and thereby promote more sensitive diagnoses, effective intervention and prevention of neonatal brain disorders.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Exploratory Neonatal Brain Disorders Research Grants, is related to the priority areas of maternal and infant health, chronic disabling conditions, and clinical preventive services. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0, or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic organizations only. The Center Director or Principal Investigator must be active in a discipline related to the study and (or) treatment of neonatal brain disorders and must demonstrate the potential for developing and directing a research program. Interrelated biomedical research projects included in the interdisciplinary research centers should be conducted by scientists who represent a variety of disciplines within basic, applied, and clinical science and from whose interactions, new scientific leads may be readily developed and effectively utilized by others. The exploratory research center program must be organized around a central research theme and must encompass plans for and development of a sufficient number of scientifically meritorious research activities to permit an effective collaborative effort among the participating investigators.

To be eligible for competition under this RFA, applicants must document the existence of, or potential for ongoing basic applied and clinical research related to neonatal brain disorders; research resources in the encompassing fields, e.g., obstetrics, perinatology, neonatology, neonatal neurology, neurological sciences, and biostatistics; clinical facilities that receive and track adequate numbers and types of neonatal and infantile neurological disabilities; cooperation among investigators within the scientific disciplines such that scientific leads may be effectively implemented; and a plan for further development of individual investigators, fellows, or clinicians in specialized techniques or procedures relevant to research on neonatal brain disorders.

## MECHANISMS OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Exploratory Grants (P20) mechanism. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. However, prospective applicants are encouraged to communicate with the NINDS program contact named in INQUIRIES, below, as early as possible in the planning stages for preparing the exploratory grant applications. The total project period for applications submitted in response to the present RFA may not exceed three years and annual direct costs of \$350,000.

This RFA is a one-time solicitation for exploratory center (P30) grants only. Future unsolicited competing applications, beyond the exploratory stage and eligible for center status, are welcome to compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

## FUNDS AVAILABLE

It is expected that up to \$1.5 million in total costs will be available for the first year of support (FY 93) to fund up to three neonatal brain disorders research center awards as a result of this announcement. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of NINDS, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## Background

Neonatal brain disorders are an important cause of mortality and morbidity contributing to the development of autism, cerebral palsy, mental retardation and a myriad of learning and developmental neurological and cognitive disabilities. Dramatic improvements in obstetrical care and treatment of neonatal respiratory disease have resulted in an increased survival of premature infants with a greater attention focused on the morbidity and mortality associated with neurological complications. Advances in fetal assessment, especially through the use of real-time ultrasound scanning, has increased our awareness of the prenatal origin of many of the neurological abnormalities detected in the newborn. It is increasingly recognized that genetic endowment, metabolic disorders, infection, environmental factors such as drugs, toxins, nutrition, intrauterine growth retardation (IUGR), and prenatal neurological insults may influence vulnerability to brain injury, intrapartum events, and postnatal outcome. New technologies such as positron emission tomography (PET), nuclear magnetic resonance spectroscopy (MRS), and near infrared spectroscopy (NIRS) available to study such disorders, as well as advances in neonatal brain research, including animal studies of mechanisms of brain injury and promising new therapies (nerve growth factors, calcium channel blockers, free radical scavengers) have provided a rapidly expanding knowledge base.

## Research Goals and Scope

It is the intent of this RFA to award exploratory grants to generate protocol planning, multidisciplinary research capacity, and pilot data as the basis for future neonatal brain research center applications. The long term goal is to develop neonatal brain research centers capable of generating complex research initiatives, answering important research questions, and providing, through the individual components, a comprehensive, integrated, and cohesive approach to neonatal brain injury. Areas of high research interest appropriate to the RFA include, but are not limited to:

- o conditions such as intracranial hemorrhage in low birthweight infants, neonatal seizures, hypoxic/ischemic encephalopathy in the pre- and full-term infant, nutrition and intrauterine growth retardation, and metabolic disorders relevant to brain development and function.
- o expanding the knowledge base of the etiology and pathogenesis of neonatal brain disorders, exploring methods to increase the capability for early and precise diagnosis, and correlating detected pathology and dysfunction with clinical course.
- o promoting an identification and understanding of the neurologically normal fetus and the high risk fetus that will allow for intrauterine and perinatal prevention of brain injury.
- o promoting the development of noninvasive neurodiagnostic techniques for assessment of neurological injury, such as NIRS and MRS, to further identify which infants may benefit from treatment intervention.
- o evaluating and refining current therapies and developing new ones, accurately assessing mortality and chronic neurologic disability with the goal of developing strategies for the prevention of the initial disorder and/or for prevention or amelioration of long-term disabilities of the nervous system.
- o experimental animal models of brain injury consistent with the neuropathological correlates in the developing human nervous system, exploring mechanisms of injury and/or therapeutic interventions.

## SPECIAL INSTRUCTIONS

## Exploratory Grants (P20)

In developing the scope of a research program that would eventually qualify for center support, applicants should base their applications on the goal of creating a clinical research center that would, at the end of an exploratory grant period, meet the qualifications contained in the Application Guidelines: Program Project and Research Center Grants (revised 06/92). These guidelines may be obtained from the program contact named in INQUIRIES, below. Therefore, the format for these exploratory grant applications should address at least the following essential components of the future center:

- o The feasibility of developing a research program centered around a unifying theme relevant to neonatal brain injury research and treatment
- o a component devoted to fundamental research of the vulnerability of developing brain to injury
- o a component devoted to clinical research on neonatal brain injury, including plans for research that may lead to the development of new therapeutic interventions, the refinement of existing forms of therapy or the preclinical testing of these forms of therapy
- o an administrative core devoted to the integration and coordination of activities within the research center and among the several research centers selected for funding.

Recognizing that in many cases the emphasis will be on future research possibilities, applicants should stress the existing and the potential strengths of the applicant organization for the development of a clinical research center. Appropriate areas may include, but are not limited to: development of additional research capabilities for basic, applied, and clinical research; potential arrangements for improved capabilities for preclinical testing of new or refined methods of diagnosis and treatment of neonatal brain disorders; potential arrangements for collaborations that would strengthen existing research interests; identification of personnel that would be considered essential for the future center and possibilities for their successful recruitment; development of plans for acquiring or providing special research and clinical skills; and possible collaborations that would ensure the availability of patients for clinical studies. This information is best



If proposed programs are expansions or modifications of existing resources or would draw upon projects currently funded under other award mechanisms or by other NIH Institutes, a mechanism should be developed for maintaining such research in a way that preserves its own identity while complementing the center, allowing for appropriate direct addition of new resources and avoiding duplication and overlap.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator names and addresses of coinvestigators responsible for each project within the center, descriptive titles of individual projects and required components, and identification of collaborating institutions.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is important in planning for the review of applications. It allows NINDS staff to estimate the potential review workload, select appropriate reviewers, and avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. Giovanna M. Spinella at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) according to instructions contained in the application kit. Application kits are available from most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441. In conjunction with the PHS 398, applicants must use the application format as described in the NINDS pamphlet, Application Guidelines: Program Project and Research Center Grants (rev. 06/92), that may be obtained from the contacts listed under INQUIRIES.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title "Exploratory Neonatal Brain Disorders Research Grants" and number must be typed in line 2a of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892 \*\*

At the time of submission, two additional copies of the application must also be sent to:

Chief, Scientific Review Branch  
Division of Extramural Activities  
National Institute of Neurological Disorders and Stroke  
Bethesda, MD 20892  
Telephone: (301) 496-9223  
FAX: (301) 401-0182

Applications must be received by April 08, 1993. If an application is received after that date, it will be returned to the applicant. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

#### REVIEW CONSIDERATIONS

Upon receipt and referral by the Division of Research Grants (DRG), applications will be reviewed by NINDS staff to determine programmatic responsiveness to this RFA. Applications judged unresponsive will be returned to the applicant. All applications that are complete and responsive may be subjected to a triage by an NINDS review group to determine relative scientific merit among the applications. The NINDS may administratively withdraw those applications judged to be noncompetitive for award. Those applications judged to be competitive for award will be further reviewed for scientific and technical merit by a peer review group convened by the NINDS. No site visits will be made. A second level of review will be carried out by the National Advisory Neurological Disorders and Stroke Council.



#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The quality of the proposed project as determined by peer review, availability of funds, and program balance among research areas of the announcement will be used in making funding decisions.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues, requests for the RFA, and requests for the NINDS pamphlet to:

Giovanna M. Spinella, M.D.  
Developmental Neurology Branch  
Division of Developmental, Convulsive, and Neuromuscular Disorders  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 820  
Bethesda, MD 20892  
Telephone: (301) 496-5821  
FAX: (301) 402-0887

Direct inquiries regarding fiscal matters to:

Gary P. Fleming, J.D.  
Grants Management Branch  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
Bethesda, MD 20892  
Telephone: (301) 496-9231

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.853, Clinical Research Related Neurological Disorders and No. 93.854, Biological Basis Research in the Neurosciences. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-150, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### GENE THERAPY APPROACHES FOR CYSTIC FIBROSIS AND OTHER HEART, LUNG, AND BLOOD DISEASES

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: HL-93-08-L

P.T. 34; K.W. 0745032, 0715040, 0715165, 0710030

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: January 25, 1993

Application Receipt Date: April 22, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) invites grant applications for support of research to develop approaches to gene therapy of diseases of interest to the NHLBI, with special emphasis on cystic fibrosis (CF). The overall objectives of this program are to advance gene therapy for cystic fibrosis and other cardiovascular, lung, and blood diseases by promoting intra- and inter-institutional collaborations, developing infrastructural resources, and fostering the entry of young and established investigators into the field of gene therapy research, as well as to promote novel, innovative pilot and feasibility studies by established gene therapy investigators.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Gene Therapy Approaches for Cystic Fibrosis and Other Heart, Lung, and Blood Diseases, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

Awards in response to this announcement will not be made to foreign institutions. Domestic applications can include an international component as a consortium arrangement if it represents a minor fraction of the total program and its unique contribution to the program is well justified.

#### MECHANISM OF SUPPORT

The support mechanism for this RFA program will be the program project grant (P01) (containing research projects and the requisite shared infrastructural resources [cores] as subcomponents under the aegis of the parent grant). Support for research projects and cores at institutions other than the parent grant can be requested as a consortium arrangement. However, because of the unique features and needs of this gene therapy program, the general requirements differ from those of the traditional program project grant. Special guidelines have been developed and are available from the program administrator listed at the end of this announcement. These instructions must be followed in responding to this RFA. The total project period for applications submitted in response to this RFA may not exceed five years. The anticipated award date is September 30, 1993. Administrative adjustments in project period and/or amount of support may be required at the time of award. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also.

Although it is expected that the investigators of the gene therapy grants will plan, direct, and execute their own research program, any substantive modifications in the program must be mutually agreed upon by the program director, the grantee institution, and the NHLBI. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to customary NIH peer review procedures.

A maximum of \$1.33 million in total costs in the 01 year with a maximum of four percent annual escalation thereafter, can be requested by the applicant. There should be at least three research projects. Core funding should not exceed 60 percent of the total cost of the grant.

This RFA program especially encourages innovative, high-risk gene therapy directions by new or established investigators through pilot/feasibility studies. Pilot/feasibility projects relevant to gene therapy of non-CF related heart, lung, and blood diseases should be submitted as a single pilot/feasibility core. Funding for such projects (limited to a maximum of \$250,000 of the total costs allotted to cores per year per parent grant) is included in the \$1.33 million total cost cap. Each pilot/feasibility project may request up to \$50,000 in total costs per year for a maximum of two years. After the two year period, additional pilot/feasibility projects may be proposed to replace those that have terminated. These pilot/feasibility projects will also be subject to the same dollar/time limits. Pilot/feasibility projects relevant to gene therapy of CF should be submitted with the application as a separate group that is clearly distinguishable from the non-CF related pilot/feasibility projects proposed. If approved for funding, these projects will be submitted to the Cystic Fibrosis Foundation (CFF) which will be responsible for their funding and management. The CFF will provide up to \$500,000 per year (direct costs) per parent grant in additional funds for this purpose (up to a maximum of five years). These funds do not count toward the \$1.33 million total cost limit set for the applications. CF pilot/feasibility projects may request up to \$50,000 per year (direct costs) for a maximum of two years. Any additional CF-related pilot/feasibility projects proposed to replace those that have terminated are subject to the same dollar/time limits.

#### FUNDS AVAILABLE

Although approximately \$4.0 million in total costs for this program is included in the financial plans for fiscal year 1993, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that three gene therapy programs will be awarded under this program.

#### RESEARCH OBJECTIVES

Complete details regarding the research objectives of this program can be found in the RFA. In brief, the overall objective of this initiative is to promote research on approaches to gene therapy for heart, lung, and blood diseases, with a special emphasis on CF, that will lead to a cure for the pulmonary manifestations of this disease. Applicants must propose, with a central focus on gene therapy of CF, a multiproject, multidisciplinary intra- and/or inter-institutional research program, comprised of the requisite infrastructural resources and core functions needed to conduct the proposed collaborative work. Pilot/feasibility studies to promote innovative, high-risk gene therapy directions by new or established investigators is encouraged.

Some areas of opportunity for research that may lead to improved gene therapy strategies for CF lung disease are cited below in order to provide a perspective of the scope of research that would meet the goals of this program.

- o Development and testing of appropriate vector (viral and nonviral) systems that will allow for effective delivery of the normal CF gene into the airway epithelium.
- o Development and testing of model systems (animal and in vitro) for evaluation of gene therapy strategies, as well as assessing safety and efficacy and for pathogenetic studies.
- o Basic cell biologic questions relevant to successful gene therapeutic approaches could include: identification of the appropriate population of airway cells to be targeted for gene therapy, the cell types expressing CFTR, the protein product of the CF gene, the stem cell and/or proliferative compartment of cells, and the effect of CFTR overexpression on cellular function.
- o Development of appropriate infrastructural resources.

It is not required that all or any of these topics be included. Investigators are encouraged to consider other relevant approaches to promoting and accelerating progress towards gene therapy for CF.

## RESEARCH OBJECTIVES

Specific areas of interest include, but are not limited to, the following:

Information on pharmacokinetics and pharmacodynamics of a drug is essential for the understanding of concentration-effect relationships and thus provides a basis for the rational design of optimum drug delivery systems. Therefore, studies specifically designed to characterize pharmacokinetics and pharmacodynamics relevant to drug delivery system development are encouraged. The development of novel assay methods for the quantification of drug concentrations in the biological systems to facilitate such pharmacokinetic/pharmacodynamic studies is also solicited. In addition, research directed at the investigation of tolerance development pertinent to the design of delivery systems for opiate agonist and partial agonist types of treatment drugs is also encouraged, as tolerance often develops rapidly under conditions of constant blood concentrations.

Controlled-release delivery systems that provide optimum drug effects by controlling the absorption rate and duration in the systemic circulation will be very useful for drug abuse treatment. Of interest is research directed at the investigation of mechanisms and factors (biological and physicochemical) that govern and affect the release rates as well as the drug absorption rates. Investigations of innovative methodology and technology based on a sound mechanistic and biological approach for the development of controlled-release drug delivery systems are encouraged. Studies are also solicited for the search for biologically relevant in vitro models or methodologies for the evaluation of these drug delivery systems.

Of particular interest among the controlled-release systems are sustained-release systems that will provide effective concentrations for a long period of time. Such systems reduce dosing frequency, and thus, not only improve treatment compliance, but also reduce the necessity for frequent clinic visits. The development of parenteral depot systems that could provide drug effects from one to two weeks is especially encouraged, since such systems also eliminate diversion problems associated with take-home doses. Transdermal systems and other systems to provide prolonged drug effects are also of interest, if the possibility of diversion could be minimized or eliminated.

Convenience of the dose administration is important in treatment clinics, particularly in view of the need to observe dosing to ensure compliance. The oral route is the most convenient means for administration. However, the duration of orally administered drugs is limited by the gastrointestinal retention time. Research directed at the development of technology to prolong the retention of medications in the gastrointestinal tract for more than 1 day is also encouraged.

Approaches for the design of pharmaceutical products that improve the bioavailability of drugs with high first-pass metabolism or significant gastrointestinal degradation are of interest. Design of innovative dosage forms to protect the drug from chemical or enzymatic degradation in the gastrointestinal tract is encouraged. Mechanistic investigations of alternate routes of administration to bypass the gastrointestinal tract, such as sublingual/buccal, rectal, and transdermal routes, are solicited.

A triggered-release system which would release the pharmacotherapeutic agent only when patients take abused drugs or when patients need it could be extremely advantageous. Applications are requested concerning an immunologically based delivery system that utilizes antigen-antibody interactions to "trigger" the system for the release of the pharmacotherapeutic agents.

Research is solicited for the development of strategies to overcome the diversion problem associated with maintenance drugs. Included are approaches for new design of pharmaceutical dosage forms such that the extraction of the active ingredient for intravenous use is prevented. Studies are also encouraged for the design of formulations that deter the diversion by incorporating an antagonist in such a manner that the antagonist, by design, via physicochemical or pharmacokinetic properties, is not bioavailable with the intended route of administration, but is bioavailable with the unintended intravenous route of administration and will, as a consequence, precipitate withdrawal.

Other novel approaches for the development of drug delivery systems with potential clinical relevance for the treatment of drug abuse will also be encouraged.

In these applications for grant funding, programmatic emphasis will be placed on innovation in design and development. To qualify for this funding program, applications should embody unique and/or innovative theoretical constructs with an experimental approach leading to a new system of drug delivery or administration or be uniquely suited to a particular pharmacotherapy in the drug abuse area.

## NIH POLICY CONCERNING INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

Applications for grants and cooperative agreements and proposals for contracts that involve human subjects are required to include minorities and both genders in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders, and conditions which disproportionately affect them. This policy applies to all research involving human subjects and human materials, and applies to males and females of all ages. If one gender and/or minorities are excluded or are inadequately represented in this research, particularly in proposed population-based studies, a clear compelling rationale for exclusion or inadequate representation should be provided. The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e.,



American Indians or Alaskan Natives, Asians or Pacific Islanders, Blacks, Hispanics). Investigators must provide the rationale for studies on single minority population groups.

Applications for support of research involving human subjects must employ a study design with minority and/or gender representation (by age distribution, risk factors, incidence/prevalence, etc.,) appropriate to the scientific objectives of the research. It is not an automatic requirement for the study design to provide statistical power to answer the questions posed for men and women and racial/ethnic groups separately; however, whenever there are scientific reasons to anticipate differences between men and women, and racial/ethnic groups, with regard to the hypothesis under investigation, applicants should include an evaluation of these gender and minority group differences in the proposed study. If adequate inclusion of one gender and/or minorities is impossible or inappropriate with respect to the purpose of the research, because of the health of the subjects, or other reasons, or if in the only study population available, there is a disproportionate representation of one gender or minority/majority group, the rationale for the study population must be well explained and justified.

The NIH funding components will not make awards of grants, cooperative agreements or contracts that do not comply with this policy. For research awards which are covered by this policy, awardees will report annually on enrollment of women and men, and on the race and ethnicity of subjects.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application from PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions.

Application kits containing the necessary forms and instructions may be obtained from the business office or office of sponsored research at most universities, colleges, medical schools, and other major research facilities. If not available from these sources, the information may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 240, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC program director or Principal Investigator should be included with the application.

#### REVIEW CONSIDERATIONS

The Division of Research Grants, NIH, serves as a central point for receipt of applications. Applications received under this announcement will be assigned to an initial review group (IRG) for scientific review in accordance with established Public Health Service Referral Guidelines. The IRGs consist primarily of non-Federal experts. Notification of the review outcome will be sent to the applicant after the initial review.

Applications will receive a secondary review for policy considerations by the appropriate National Advisory Council. Only applications recommended for further consideration by Council may be considered for funding.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to the Institute. Applications recommended for further consideration by the appropriate National Advisory Council will be considered for funding on the basis of overall scientific and technical merit of the application as determined by peer review, Institute program needs and balance, and availability of funds.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the Program Announcement to:

C. Nora Chiang, Ph.D.  
Chemistry and Pharmaceuticals Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 11A55  
Rockville, MD 20857  
Telephone: (301) 443-5280



Direct inquiries regarding fiscal matters to:

Shirley Denney  
Office of Planning and Resource Management  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.279. Awards are made under the authorization of the Public Health Service Act, sections 301 and 515 (42 U.S.C 241 and 290cc) and administered under PHS grants policies and Federal Regulations 42 CFR 92 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 as implemented under Department of Health and Human Services regulations at 45 CFR Part 100 or Health Systems Agency review. Special attention is called to 42 CFR Part 2, Confidentiality of Alcohol and Drug Abuse Patient Records.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***

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# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 39, Part II of II  
October 30, 1992

RICHARD W MURRY

# 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

NOTICES OF AVAILABILITY (RFPs AND RFAs)

INTERACTIVE RESEARCH PROJECT GRANTS FOR NUTRITION AND CANCER PREVENTION

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: CA-93-04

P.T. 34; K.W. 0710095, 0715035, 0745027

National Cancer Institute, Division of Cancer Prevention and Control

Letter of Intent Receipt Date: November 24, 1992  
Application Receipt Date: January 19, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

PURPOSE

The Division of Cancer Prevention and Control, National Cancer Institute (NCI), invites Interactive Research Project Grants (IRPGs) to encourage and facilitate formal interdisciplinary collaborations through the coordinated submission of related research project applications that share a common research focus relevant to nutrition and cancer prevention but do not require extensive shared physical resources or core functions.

A minimum of three independent investigators with related research objectives are encouraged to submit concurrent, collaborative, cross-referenced individual research project grant applications (R01) that share a common research focus. Applications may be submitted from either a single institution or a consortium of institutions. Applications will be reviewed independently for scientific merit. Meritorious applications will be considered for funding both as independent awards and in the context of the overall proposed collaboration.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000", a PHS-led national activity for setting priority areas. This RFA, Interactive Research Project Grants for Nutrition and Cancer Prevention, is related to the priority area of cancer prevention. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-0043-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (Telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Domestic and foreign non-profit and for-profit organizations and institutions, governments and their agencies are eligible to apply. Applications may be submitted from a single institution or may include arrangement with multiple institutions if appropriate. Applications from or involving minority institutions, individuals and women are encouraged.

Each application will be considered on its own merit as an individual research project. Therefore, applicants for IRPGs MAY NOT concurrently submit R01 applications that represent significant duplication of the efforts described in the applicant's IRPG. In this regard, it should be noted that the NCI will consider funding meritorious individual IRPG applications if it is not possible to fund the IRPG package as a whole. Concurrent submission of program project (P01) applications that request support for essentially similar work is prohibited.



## MECHANISM OF SUPPORT

Support of this program will be by the research project (R01) grant. Applicants will be responsible for the planning, direction and execution of the proposed projects. The total project period for applications submitted in response to the RFA should not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to customary peer review.

## FUNDS AVAILABLE

Approximately \$2.5 million in total costs per year for up to five years will be committed to specifically fund applications that are submitted in response to this RFA. It is anticipated that six to nine awards will be made. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided or in the financial plans of the NCI, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

## RESEARCH OBJECTIVES

The objectives of this RFA for Interactive Research Project Grants are (1) to increase the investigator-initiated pool of quality applications in the area of nutrition and cancer research and (2) to stimulate an intermediate level of interdisciplinary collaborative efforts to build stronger research bridges between nutritional science and the disciplines that relate closely to basic and clinical research for the development and evaluation of new approaches to nutrition and cancer prevention research.

### Research Areas of Interest

Representative areas of particular interest for this RFA focus on innovative research approaches for the development, evaluation and/or application of specific methodologies for elucidating the mechanisms of action and quantification of the role of diet and dietary components in cancer prevention.

Several examples of research areas relevant to nutrition and cancer prevention in which the IRPG concept may be applied are as follows:

- o Metabolic effectors of dietary origin. Basic science projects may be combined that integrate multiple aspects of dietary factors that modulate signal transduction, DNA repair, antioxidants, hormonal regulation and gene regulation.
- o Interaction of diet and dietary components with drugs, hormones, metabolites and genes - synergistic and antagonistic effects.
- o Development of new and better methods to quantify dietary intake in individuals.
- o Further identification and evaluation of overall dietary patterns, foods and food constituents that alter cancer risk and elucidation of their mechanisms of action.
- o Identification of markers of dietary exposure and early indicators of risk.
- o Quantification of optimal ranges of dietary constituents that affect cancer risk.
- o Social behavioral research to identify motivation factors and barriers to changing food habits.
- o Nutrition as one component of healthy lifestyle modification. Studies of fundamental relationships between diet, nutrition and cancer and behavioral change affiliated with modification.

Prospective applicants are encouraged to explore other areas of potential for the Interactive Research Project Grant mechanism with the NCI Program Director.

The overall goal is to provide more definitive data for developing quantitative dietary guidance and translation into optimal and desirable eating patterns and food choices that have the potential for a substantial reduction in the risk of diet-related cancers in the general population.

All PHS and NIH grants policies will apply to applications received in response to this RFA.

## STUDY POPULATIONS

### SPECIAL INSTRUCTION TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by November 24, 1992, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, it is requested in order to provide an indication of the number and scope of applications to be reviewed.

The letter of intent is to be sent to:

Carolyn K. Clifford, Ph.D.  
Diet and Cancer Branch  
Division of Cancer Prevention and Control  
National Cancer Institute  
Executive Plaza North, Room 212  
Bethesda, MD 20892-6130  
Telephone: (301) 496-8573  
FAX: (301) 402-0553

#### APPLICATION PROCEDURES

The research grant application form PHS-398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441; and from the NCI Program Director named below.

#### SPECIAL INSTRUCTIONS FOR IRPG APPLICATIONS

The NCI encourages qualified investigators to develop and submit concurrently coordinated research project applications that address areas of relevance to nutrition and cancer prevention where the interactive research project concept may be applied. Applications submitted as a package should be tightly focused and the interactions and benefits of the proposed linkages should be made explicit as described in the RFA. One Principal Investigator from the IRPG group MUST be identified as the "Program Coordinator", and should be cited in all applications on Page 2 of PHS Form 398 (revised 9/91). Individual investigators may request funds for the time and effort contributed toward the coordination of the overall research and for collaborative resource activities. Other required applicant information and special instructions for preparation of IRPG applications are also included in the RFA that is available on request from the NCI Program Director cited in INQUIRIES, below.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed (initially) by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the program requirements and criteria stated in the RFA is an NCI program staff function. Questions concerning the responsiveness of proposed research to the RFA may be directed to the Program Director named under INQUIRIES.

If the number of applications is large compared to the number of awards to be made, the NCI may conduct a preliminary scientific peer review to eliminate those applications that are clearly not competitive. The NCI will remove from competition those applications judged to be noncompetitive for award and notify the applicant and institutional business official. Those applications judged to be both competitive and responsive will be further evaluated according to the review criteria stated below for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board considers the special needs of the NCI and the priorities of National Cancer Program.

#### AWARD CRITERIA

The anticipated date of award is September 30, 1993. Although this program is provided for in the financial plans of the NCI, awards made pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA, inquiries about whether or not specific proposed research would be responsive are encouraged and may be directed to the Program Director listed below. The program staff welcome the opportunity to clarify any issues or questions from potential applicants.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Carolyn K. Clifford, Ph.D.  
Program Director, Diet and Cancer Branch  
Division of Cancer Prevention and Control  
National Cancer Institute  
Executive Plaza North, Suite 212  
Bethesda, MD 20892-6130  
Telephone: (301) 496-8573  
FAX: (301) 402-0553

Direct inquiries regarding fiscal matters to:

Eileen Natoli  
Team Leader, PC Team  
Grants Administration Branch

National Cancer Institute  
6120 Executive Boulevard  
Executive Plaza South, Room 243  
Rockville, MD 20852  
Telephone: (301) 496-7800 Ext.56

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.399, Cancer Control. Awards will be made under the authority of the Public Health Services Act, Title IV, Section 301 (Public Law 78-410, 42 U.S.C. 241 and Section 412, as amended by Public Law 99-518, 42 U.S.C 258a-1); and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12732 or Health Systems Agency review.

#### PROGRAM PROJECTS ON TRANSPLANTATION IMMUNOLOGY AND IMMUNOGENETICS

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: AI-93-01

P.T. 34; K.W. 0710065, 0710125, 0705040

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: December 15, 1992

Application Receipt Date: March 10, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Allergy, Immunology and Transplantation, National Institute of Allergy and Infectious Diseases (NIAID), invites applications for Program Projects on Transplantation Immunology and Immunogenetics. The ultimate goal of the research to be conducted is to achieve the ability to induce a long lasting unresponsiveness that is specific for the organ/tissue donor as well as for the recipient of transplanted immuno-competent tissues. The objective of the research should be to characterize the regulatory mechanisms involved in allorecognition and responsiveness and to utilize this information to develop approaches toward induction of a donor- (or host-, where relevant) specific non-responsive state. This program is intended to stimulate collaboration among transplant clinicians, clinical scientists, basic immunologists and immunogeneticists in studies of the immune system attendant to allogeneic transplantation. Such studies may involve: identification and characterization of genetic elements regulating the allogeneic response; elucidation of the cellular and molecular mechanisms involved in both the induction and effector phases of the allogeneic response; evaluation of the relevance of graft rejection or graft-versus-host disease to the development of donor-specific energy or tolerance; characterization of the mechanisms by which donor lymphoid tissue induces an allogeneic response and its potential role in the development of long-term non-responsiveness; and the development of therapeutic procedures for inducing long-term graft survival. This RFA is a reannouncement with modified scope of RFA AI-91-14 published in the NIH Guide for Grants and Contracts, Vol. 20, No. 33., September 6, 1991, Additional reannouncement is possible in the future depending on programmatic needs in this area and the availability of funds.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Program Projects on Transplantation Immunology and Immunogenetics, is related to the priority area of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Foreign organizations are not eligible to apply. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Program Project (P01) grant mechanism. The P01 is an assistance mechanism for the support of broadly based, multidisciplinary, long-term research programs with a specific major goal or basic theme and generally involving the organized efforts of groups of investigators. Applicants will be solely responsible for the planning, direction, and execution of the proposed projects. The total project period for applications submitted in response to the RFA may not exceed five years. The anticipated date of award is September 1993. Budget requests should be limited to no more than \$500,000 total direct costs per annum. Budget requests exceeding this amount will require approval by senior NIAID officials through the program officer before the application is accepted for review.



The estimated total funds available (direct and indirect costs) for the first year for successful applications in response to this RFA is \$1,500,000. In Fiscal Year 1993, the NIAID plans to award at least two program project grants submitted in response to this RFA and, depending on availability of funds and scientific merit, possibly more than two. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIAID, awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and availability of funds.

#### RESEARCH OBJECTIVES

The purpose of this RFA is to stimulate collaboration among transplant clinicians, clinical scientists, basic immunologists and immunogeneticists in studies of the immune system in allogeneic transplantation. Emphasis should be placed on the application of up-to-date concepts and techniques to evaluate of the immune system in to the allogeneic transplantation. Applicants are encouraged to emphasize: new ideas and innovative research approaches likely to lead to the acquisition of new knowledge about the immune system's ability to respond to the graft; methods to specifically suppress the immune system without totally immunocompromising the recipient; the state of the immune system under current immunosuppressive protocols; and the immune system's ability to respond to natural and test agents. While the NIAID stresses the translation of basic research to clinical applications, preclinical studies involving laboratory animals are encouraged.

The objective of the research should be to characterize the regulatory mechanisms of allorecognition and the use of this information to develop approaches toward induction of a donor- (or host-, where relevant) specific non-responsive state. These studies could include an evaluation of the immune status of the transplant recipient both prior to and after transplantation and should be directed at characterizing the specific mechanisms responsible for observed changes.

Appropriate approaches emphasizing the induction of clinical tolerance/antigen specific unresponsiveness leading to the long-term survival of organ allografts are stressed. These might include, but are not restricted to, investigations of:

- o the cellular and molecular mechanisms responsible for the induction of the immune response to organ allografts and the modification of this response with agents which act on: macrophages (or their organ specific equivalents); specific T-cell subsets; T-cell products (e.g., lymphokines) and cell surface receptors (e.g., the IL-2 receptor);
- o molecular genetic manipulation of specific lymphocyte populations for in vivo therapeutic procedures;
- o characterization of the regulatory interactions between different populations of lymphocytes (a) of the host in reactivity against donor tissue; (b) of the donor in graft versus host reaction; and (c) of both donor and recipient in situations which involve two-way cell trafficking;
- o the utilization of anti-idiotypic reagents in the regulation of the immune response to allografts; and
- o identification of minor histocompatibility systems and measurement of their impact on rejection.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women and minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by December 15, 1992, a letter of intent that includes a descriptive title of the overall proposed research, the name, address and telephone number of the Principal Investigator, a list of the names of key investigators and their institution(s), and the number and title of this RFA. Although the letter of intent is not required, is not binding, does not commit the sender to submit an application, and does not enter into the review of subsequent applications, the information that it contains allows NIAID staff to estimate the potential review workload and to avoid conflict of interest in the review. The letter of intent is to be sent to Dr. Mark Rohrbach at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted on the standard research grant application form PHS 398 (rev. 09/91). For purposes of identification and processing, item 2a on the face page of the application should be marked "yes" and the RFA number and the words "Program Projects on Transplantation Immunology and Immunogenetics" must be typed in.

These forms may be obtained from most institutional sponsored research offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441; and from Dr. Mark Rohrbach at the address listed under INQUIRIES.

Applications must be received by March 10, 1993.



## REVIEW CONSIDERATIONS

General review considerations are outlined in the NIAID Information Brochure on Program Projects and Centers (which also is applicable to Cooperative Agreements), which contains special instructions for preparing multiproject applications for Program Projects. It includes REVIEW PROCEDURES and REVIEW CRITERIA for multicomponent interdisciplinary projects and other important information. This Brochure and the RFA will be sent to applicants upon request. Additional review criteria are outlined in the RFA.

Upon receipt, applications will be reviewed for completeness by the NIH DRG and for responsiveness by NIAID staff; those judged to be incomplete or non-responsive will be returned to the applicant without review.

Those applications that are complete and responsive may be subjected to a triage by an NIAID peer review group before or during the scientific review meeting to determine their scientific merit relative to other applications received in response to this RFA. The NIAID will withdraw from competition those applications judged to be non-competitive for award and will notify the applicant and institutional business officials.

Those applications judged by the reviewers to be competitive for award will be further reviewed for scientific and technical merit by a review committee convened by the Division of Extramural Activities, NIAID, during June 1993. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council in September 1993. September 1993 will be the earliest starting date for successful applicants.

## AWARD CRITERIA

The earliest anticipated date of award is September 1993. Funding decisions will be made on the basis of scientific and technical merit as determined by peer review, program needs and balance, and the availability of funds.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcomed.

Direct requests for the RFA, the NIAID Information Brochure on Program Projects, and inquiries regarding programmatic issues to:

Andrea A. Zachary, Ph.D., Chief, Transplantation Section  
Genetics and Transplantation Branch  
Division of Allergy, Immunology and Transplantation  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4A13  
Bethesda, MD 20892  
Telephone: (301) 496-5598  
FAX: (301) 402-0175

Direct inquiries regarding review issues and send the Letter of Intent to:

Mark Rohrbach, Ph.D.  
Microbiology & Immunology Review Section  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C22  
6003 Executive Boulevard  
Bethesda, MD 20892 (Rockville, 20852 if using overnight delivery services)  
Telephone: (301) 496-8424  
FAX: (301) 402-2638

Direct inquiries regarding fiscal matters to:

Mr. Jeffrey Carow  
Chief, Immunology Grants Management Section  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B29  
Bethesda, MD 20892  
Telephone: (301) 496-7075

## Schedule

Letter of Intent Date:	December 15, 1992
Application Receipt Date:	March 10, 1993
Scientific Review Date:	June 1993
Advisory Council Date:	September 1993
Earliest Award Date:	September 1993

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.855, Immunology, Allergy and Transplantation Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal

ISCHEMIC HEART DISEASE, SUDDEN CARDIAC DEATH, HEART FAILURE

NIH GUIDE, Volume 21, Number 39, October 30, 1992

RFA AVAILABLE: HL-93-06-H

P.T. 04; K.W. 0715040, 0755030, 0765035, 0710030, 0745020, 0745027

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: June 1, 1993

Application Receipt Date: August 2, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAIN ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

PURPOSE

This initiative seeks to foster an innovative research approach to the study of Ischemic Heart Disease, Sudden Death, or Heart Failure. This will be accomplished by soliciting applications for Specialized Centers of Research (SCOR) for each of these three diseases. The program is open to all investigators, including those who are participating in the current SCOR program and those who are not. The emphasis of this new solicitation is on creative, interdisciplinary approaches to elucidation of the etiology and pathophysiology of these diseases at the molecular, cellular, and tissue levels and the translation of research findings into improved diagnosis, treatment and prevention. Applicants are required to select a single theme pertaining to Ischemic Heart Disease or Sudden Cardiac Death or Heart Failure and to develop a cluster of research projects clearly focussed on that theme. The goal is to foster a synergistic environment for integrating basic science and clinical investigations. All projects must have clearly stated hypotheses and include original and innovative ideas with respect to the problem to be studied.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. The RFA, Specialized Centers of Research in Ischemic Heart Disease, Sudden Cardiac Death, and Heart Failure, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit, and non-profit organizations, public and private, such as universities, units of State and local governments, and eligible agencies of the Federal government that have established clinical programs in cardiology and the capability to conduct relevant basic research. Applications from minority individuals and women are encouraged. Foreign organizations are ineligible. International collaborations in domestic applications will only be accepted if the resources are clearly shown to be unavailable to the U.S.

The Program Director must be willing to devote at least 25 percent effort to the SCOR and must be a project leader on at least one project or core. All other project leaders must devote at least 20 percent effort to their projects.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) specialized center grant mechanism (P50). Responsibility for planning the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years. The anticipated date of award is January 1, 1995. Since a variety of approaches would represent valid responses to this announcement it is anticipated that there will be a range of costs among individual grants awarded.

This RFA will be the final solicitation for the area of ischemic heart disease.

FUNDS AVAILABLE

Approximately \$18 million in total cost will be provided for the first year of support for the entire program. However, no applicant may request more than \$1 million in direct costs in the first year of support. Indirect costs associated with subcontracts are not included in calculations of the upper limit. Future years may be escalated at no more than four percent. It is anticipated that 10-12 grants will be awarded under this program. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the NHLBI, awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Administrative adjustments in project period and/or amount of support may be required at the time of the award.

RESEARCH OBJECTIVES

The goal of this program is reduction of morbidity and mortality due to ischemic heart disease, sudden cardiac death, and heart failure by fostering collaborations between basic and clinical investigators.

## Ischemic Heart Disease

Appropriate topics include, but are not limited to, improved strategies to assess myocardial perfusion and viability, the physiologic basis for chest pain and silent ischemia, the cardiac microcirculation, and mechanisms underlying restenosis and reperfusion injury and methods for prevention.

## Sudden Cardiac Death

A concerted effort is required by basic and clinical investigators to devise methods to identify patients at risk and to develop new preventive strategies. Research is needed to acquire knowledge of the precipitating mechanisms that lead to the lethal event and to identify the substrate with which the precipitating factor interacts. Metabolic, genetic, electrophysiologic, and neural factors are among those that may contribute to susceptibility to sudden cardiac death.

## Heart Failure

The goal of this program is to correlate clinical findings with the molecular and cellular mechanisms that lead to heart failure, to use that knowledge to devise new methods for treatment, and to discover whether or not earlier diagnosis through more sensitive imaging techniques or biochemical markers could result in more effective preventive measures.

## SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by June 1, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the principal investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications.

The letter of intent is to be sent to:

Chief, Centers and Special Projects Section  
Review Branch/Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 553A  
Bethesda, MD 20892

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Applicants must follow the instructions provided in the supplement to the RFA.

## REVIEW CONSIDERATIONS

Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NHLBI. The second level of review will be provided by the National Heart, Lung, and Blood Advisory Council.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications, with added criteria evaluating the interaction between clinical and basic investigators and the overall merit of the program as a whole.

## AWARD CRITERIA

Applications must fulfill all the eligibility criteria in order to be considered for funding. The most important criterion in selecting awardees will be the scientific merit as reflected in the priority score. However, factors such as program balance and available funds may enter into selection from among meritorious applications.

## INQUIRIES

Inquiries regarding this announcement and requests for the RFA may be directed to:

Dr. Constance Weinstein  
Cardiac Diseases Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3C06

Bethesda, MD 20892  
Telephone: (301) 496-1081  
FAX: (301) 480-6282

Inquiries regarding fiscal and administrative matters may be directed to:

Mr. William Darby  
Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A11  
Bethesda, MD 20892  
Telephone: (301) 496-7536  
FAX: (301) 402-1200

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### NIH LOAN REPAYMENT PROGRAM FOR AIDS RESEARCH

NIH GUIDE, Volume 21, Number 39, October 30, 1992

PA NUMBER: PA-93-013

P.T. 34; K.W. 0715008, 1014006

National Institutes of Health

Application Receipt Dates: January 19, April 26, and July 26, 1993

#### PURPOSE

This notice is a republication, with significant modifications, of a previous issuance on this subject (NIH Guide, Vol. 21, No. 27, July 31, 1992). It is being reissued to emphasize the availability and to provide updated information regarding expanded eligibility criteria.

On November 4, 1988, the United States Congress enacted Public Law 100-607, directing the National Institutes of Health (NIH) to establish a program of educational loan repayment to attract additional investigators into Acquired Immunodeficiency Syndrome (AIDS) research. The NIH Loan Repayment Program for AIDS Research (LRP), to increase the number of investigators conducting AIDS research at the NIH, invites interested health professionals to apply for LRP participation.

The LRP may pay a maximum of \$20,000 a year directly to a participant's lenders for qualifying educational debt during an initial, minimum two-year service period. The actual loan repayment is based, in part, on the availability of funding as well as the proportion of the participant's qualifying debt relative to their NIH basic pay or stipend. Since such payments to lenders are considered income for the participant and increases his/her Federal tax liability, the LRP also makes payments, equal to 39 percent of the total loan repayments, directed towards the participant's Internal Revenue Service (IRS) account. The LRP may make additional tax reimbursements to those participants who show an increase in State and/or local tax liability. Benefits are paid in addition to a participant's annual NIH basic pay or stipend.

As of October 1, 1992, the NIH has been expanded to include three additional research institutes that were formerly components of the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA): National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Drug Abuse (NIDA), and National Institute of Mental Health (NIMH). Therefore, qualified employees of NIAAA, NIDA, and NIMH, as of October 1, 1992, are considered NIH employees and eligible for LRP participation subject to the other criteria and procedures described herein.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, NIH Loan Repayment Program for AIDS Research, is related to the priority area of HIV infection. Those interested may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

An applicant to the LRP is accepted for LRP participation when his/her qualified AIDS research assignment is approved by the AIDS Research Loan Repayment Committee (LRC) and his/her contract is executed. Specific LRP applicant and participant eligibility criteria include the following:

1. Individuals employed by the NIH during the period November 4, 1987, through November 3, 1988, are INELIGIBLE;



2. Applicants must be citizens or permanent residents of the United States;
3. Applicants must have a Ph.D., M.D., D.O., D.D.S., D.M.D., D.V.M., or equivalent degree;
4. Applicants must have qualified educational debt in excess of 20 percent of their annual NIH basic pay or stipend on the date of program eligibility, resulting from governmental or commercial loans obtained to support their undergraduate and/or graduate education;
5. Individuals with existing service obligations to Federal, State, or other entities will NOT be considered for the LRP unless deferrals are granted for the length of their LRP service obligation;
6. Applicants must be appointed under a temporary or permanent employment mechanism that allows their employment with the NIH to last a minimum of two years;
7. Individuals who are not NIH employees, such as Visiting Fellows, Intramural Research Training Award (IRTA) recipients, National Research Service Award (NRSA) recipients, Guest Researchers or Special Volunteers, NIH National Research Council (NRC) Biotechnology Research Associates Program participants, and Intergovernmental Personnel Act (IPA) participants, may NOT participate in the LRP; and
8. Applicants will NOT be excluded from consideration under the LRP on the basis of race, color, creed, religion, sex, handicap, age, national origin, or political affiliation.

In addition, to qualify for repayment, LRP applicants' debts are subject to the following limitations and restrictions:

The LRP will repay lenders for the principal, interest, and related expenses (such as the required insurance premiums on the unpaid balances of some loans) of qualified Government (Federal, State, and local) and commercial educational loans obtained by participants for the following: (1) undergraduate, graduate, and health professional school tuition expenses; (2) other reasonable educational expenses required by the school(s) attended, including fees, books, supplies, educational equipment and materials, and laboratory expenses; and (3) reasonable living expenses, including the cost of room and board, transportation and commuting costs, and other reasonable living expenses as determined by the LRP.

The following loans are NOT repayable under the LRP: (1) loans not obtained from a Government entity or commercial lending institution, such as loans from friends, relatives, or other private individuals; (2) loans for which contemporaneous documentation is not available; (3) loans or portions of loans obtained for educational or living expenses that exceed the "reasonable" level as determined by the standard school budget for the year in which the loan was made, and are not determined by the LRP to be reasonable based on additional documentation provided by the applicant; and (4) loans, financial debts, or service obligations incurred under the Physicians Shortage Area Scholarship Program, National Research Service Award Program, Public Health and National Health Service Corps Scholarship Training Program, National Health Service Corps Scholarship Program, Armed Forces (Army, Navy, or Air Force) Health Professions Scholarship Program, and Indian Health Service Scholarship Program.

Loans in default and loans not current in payment schedule, will not be considered as qualifying for repayment. Repayments will only be made for loans with current payment status. During lapses in loan repayments, due either to program administrative complications or a break in service, participants are wholly responsible for making payments or any other arrangements that maintain loans in a current payment status. Penalties assessed to participants as a result of LRP administrative failures to maintain current payment status may be considered for reimbursement.

Payments will NOT be made under the LRP for loans that participants have paid prior to the program eligibility date.

#### RESEARCH OBJECTIVES

The LRP is designed to attract additional investigators into AIDS research. The LRP intends to fund individuals conducting AIDS research as described in the following paragraphs that contain the "Activities Constituting AIDS Research" criteria as adopted by the LRC on October 13, 1992:

"The following parameters define whether or not a proposed research assignment meets the criteria for coverage under the NIH Loan Repayment Program for AIDS Research - that is, whether or not the incumbent will be "primarily" engaged in AIDS research. "Primarily" engaged in AIDS research is defined as AIDS research activities that constitute at least 80 percent of a researcher's time. Clinical Associates, whose intent is to primarily engage in AIDS research, must engage in qualified AIDS research for at least three months in the first year of their program, with a total of fifteen months of qualified AIDS research during their two-year contract.

"AIDS research includes studies of the human immunodeficiency virus (HIV), the pathophysiology of HIV infection, the development of models of HIV infection and its sequelae, cofactors predisposing to HIV infection and AIDS, or its sequelae, and the development of vaccines and therapeutics. More specifically, the following research activities are included: (1) studies of HIV and related retroviruses; (2) studies of the mechanism(s) by which HIV and related retroviruses establish infection and infect host cells; (3) studies of the mechanism(s) by which HIV and related retroviruses cause disease, including studies of the immune deficiency induced by HIV and related retroviruses; (4) studies of the pathophysiology of host response to HIV infection; (5) studies of in vivo or in vitro models of human HIV infection and its sequelae; (6) epidemiologic studies of HIV and related retrovirus infection; (7) clinical trials involving prophylaxis or therapy for HIV infection or its sequelae; (8) preclinical studies aimed at the development of therapy for or prevention of HIV infection and the immunodeficiency caused by HIV infection and its sequelae; (9) cofactors predisposing to acquiring HIV infection and/or the progression of HIV-related disease; (10) basic studies and clinical trials involving vaccines, or other immunological or chemotherapeutic interventions for the prevention of HIV infection and its sequelae; (11) studies into the transmission of HIV involving high risk behaviors and research concerning the interruption of

transmission by behavioral change and pharmacologic intervention; and (12) basic studies of the societal impact of and response to the HIV/AIDS epidemic, including subgroups within the population.

"AIDS researchers include scientists who are intellectually engaged in the process of providing scientific direction and guidance in programs of original AIDS research, specifically epidemiologists, statisticians, and others who are involved in the design and conduct of research studies. The duties of such scientists may include the generation and design of studies and the collation and analysis of data; and/or the preparation and publication, as author or co-author, of studies in peer-reviewed journals.

"AIDS researchers also include physicians who are providing care for HIV-infected individuals who are subjects of HIV-related research."

#### APPLICATION PROCEDURES

An initiating official, which may be a laboratory or branch chief, must recommend an individual to the LRP, and the Institute, Center, or Division (ICD) Scientific Program Director and ICD Director must concur. Since LRP participation is contingent, in part, upon employment with the NIH, candidates may not be recommended for loan repayment by an ICD until a firm employment commitment has been made by the recommending ICD's Personnel Department.

ICD Loan Repayment Program Coordinators forward recommended applications to the Director, LRP, who submits eligible applications for consideration and approval/disapproval by the LRC. Recommended candidates may forward financial information directly to the Director, LRP.

At the conclusion of the initial contract, participants may reapply and be considered for subsequent, one-year continuation contracts. Continuation contracts are based upon the same review criteria as the initial contract, in addition to a submission that describes AIDS research accomplishments made during the initial contract. These continuation contracts are approved on a year-to-year basis and are contingent upon the appropriation and availability of funds.

#### REVIEW PROCEDURES

The LRC reviews the scientific research portions of eligible LRP applications. The LRC, which is composed of intramural and extramural scientific staff, reviews, ranks, and approves or disapproves applications. LRC approval, in part, is based on the appropriateness of the research assignment to the LRP's AIDS research criteria (see above) and the scientific merit of the research. In addition, the credentials provided in the application are reviewed and ranked to assess the applicant's potential to conduct qualified AIDS research.

LRP program staff review and verify the financial portions of eligible applications and determine projected funding levels. Actual funding is dependent upon LRC approval and the terms of the LRP service contract.

#### AWARD CRITERIA

The award of funds for approved applications is contingent, in part, upon the availability of funds appropriated by the Congress of the United States for the NIH. Funds will not be awarded to disapproved applications. In return for the repayment of their educational loans, participants must agree to: (1) be "primarily" engaged in qualified AIDS research, which is described above in the "Activities Constituting AIDS Research" criteria, as NIH employees for a minimum period of two years; (2) make payments to lenders on their own behalf for periods of Leave Without Pay (LWOP); (3) pay monetary damages as required in cases where the initial contract is breached; and (4) all other provisions agreed upon in their contracts. Substantial monetary penalties will be imposed for breach of contract.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome. Information regarding the LRP may be obtained by calling or writing:

Marc S. Horowitz, J.D.  
Director, NIH Loan Repayment Program for AIDS Research  
Office of AIDS Research  
National Institutes of Health  
Building 31, Room 5C12  
Bethesda, MD 20892  
Telephone: (800) 528-7689

#### AUTHORITY AND REGULATIONS

The LRP is described in the Catalog of Federal Domestic Assistance No. 93.936. Awards are made under authorization of section 487A of the PHS Act (42 U.S.C. 288-1), as amended by section 634 of the Health Omnibus Programs Extension of 1988 (P. L. 100-607). This program is not subject to the provisions of Executive Order 12372, Intergovernmental Review of Federal Programs, and was granted clearance from the Office of Management and Budget (OMB) (0925-0361), under the requirements of the Paperwork Reduction Act of 1980, on June 15, 1990.

# NIH GUIDE

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## For Grants and Contracts

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**National Institutes of Health Room B4BN23,**  
**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21., No. 40  
November 6, 1992

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

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GAITHERSBURG MD 20879 0000





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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

# NOTICES

## THE ETHICS OF CLINICAL RESEARCH ON HUMAN SUBJECTS: FACING THE 21st CENTURY

NIH GUIDE, Volume 21, Number 40, November 6, 1992

P.T. 42; K.W. 0783005

National Institutes of Health

The National Institutes of Health (NIH) Office for Protection from Research Risks (OPRR) is co-sponsoring with the University of Texas Medical Branch, Galveston a conference to discuss the ethical issues associated with clinical research involving human subjects. This conference is open to anyone with an interest in research involving human subjects and may be of special significance for individuals serving on Institutional Review Boards.

DATES: February 28 through March 2, 1993

LOCATION: San Luis Hotel  
5222 Seawall Boulevard  
Galveston, TX 77551  
Telephone: 1-800-392-5937

SPONSORS: The University of Texas Medical Branch at Galveston Galveston, Texas  
National Institutes of Health, Office for Protection from Research Risks, Bethesda, MD

REGISTRATION AND INFORMATION: Ms. Sharon Goodwin  
Institute for the Medical Humanities  
301 University Boulevard, M-11  
The University of Texas Medical Branch  
Galveston, TX 77555-1311  
Telephone: (409) 772-2376

This national/international conference will explore the ethics of clinical research on human subjects. The goals of this timely meeting include:

- (1) providing a forward-looking analysis of the major ethical issues now facing biomedical researchers and institutions;
- (2) critically examining research ethics as set forth in the Belmont Report and other position papers of the two National Commissions;
- (3) enabling researchers and research-oriented administrators to plan effectively for future research initiatives; and
- (4) providing a forum for discussion and collaboration between IRB members and ethicists.

#### INQUIRIES

Ms. Roberta Sonneborn  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-7163

#### NATIONAL HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 40, November 6, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

#### SOUTHWESTERN WORKSHOP

DATES: November 16 and 17, 1992

#### LOCATION:

Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

#### SPONSORS:

University of Texas Health Science Center at Houston  
Prairie View A&M University

#### REGISTRATION:

Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

TITLE: Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

DESCRIPTION: Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, and other health care professionals, clergy, lawyers, medical, nursing, social work students, psychologists, and IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

#### SOUTHEASTERN WORKSHOP

DATES: January 14 and 15, 1993

NIH Guide for Grants and Contracts - Vol. 21, No. 40 - November 6, 1992

LOCATION:  
Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

SPONSORS:  
University of South Florida  
Florida A & M University

REGISTRATION:  
Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks--medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

#### SOUTHWESTERN WORKSHOP

DATES: February 12 and 13, 1993

LOCATION:  
Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

SPONSORS:  
Arizona State University  
Northern Arizona University

REGISTRATION:  
Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

TITLE: Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

DESCRIPTION: This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

#### SOUTHWESTERN WORKSHOP

DATES: February 28 through March 2, 1993

LOCATION:  
San Luis Hotel  
5222 Seawall Boulevard  
Galveston, TX 77551  
Telephone: (800) 392-5937

**SPONSORS:**

The University of Texas Medical Branch at Galveston

**REGISTRATION:**

E. Ray Stinson, Ph.D.  
Office of Sponsored Programs-Academic  
The University of Texas Medical Branch at Galveston  
Galveston, TX 77555-1311  
Telephone: (409)-772-3482

**TITLE:** The Ethics of Clinical Research on Human Subjects: Facing the 21st Century

For further information regarding these workshop and future NIH/FDA National Human Subject Protections Workshops, please contact:

Ms. Darlene Marie Ross  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

**WORKSHOP ON MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS**

**NIH GUIDE**, Volume 21, Number 40, November 6, 1992

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health (NIH), Office for Protection from Research Risks (OPRR), is continuing to sponsor workshops on implementing the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Each of the workshops scheduled for FY 1993 will focus on a specific theme.

The workshops are open to institutional administrators, members of Institutional Animal Care and Use Committees, laboratory animal veterinarians, investigators and other institutional staff who have responsibility for high-quality management of sound institutional animal care and use programs.

Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR representatives.

**DATE:** DECEMBER 3-4, 1992

**TOPIC:** MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

**LOCATION:**

Loews Vanderbilt Plaza  
2100 West End Avenue  
Nashville, TN 37203  
Telephone: (615) 320-1700  
FAX: (615) 320-5019

**SPONSORS:**

Vanderbilt University  
Meharry Medical College

**REGISTRATION:**

Ms. Marilyn Dasaro  
Division of Continuing Medical Education  
Vanderbilt University  
D-8211 Medical Center North  
Nashville, TN 37232-2337  
Telephone: (615) 322-4030  
FAX: (615) 343-0809

**DATE:** JANUARY 21-22, 1993

**TOPIC:** TO BE ANNOUNCED

**LOCATION:**

Sheraton Grande Torrey Pines  
10950 N. Torrey Pines Road  
La Jolla, CA 92037  
Telephone: (619) 558-1500  
FAX: (619) 558-1131

**SPONSORS:**

Scripps Clinic and Research Foundation  
Salk Institute



REGISTRATION:  
Janie Partridge  
Scripps Clinic and Research Foundation/MB  
10666 North Torrey Pines Road  
La Jolla, CA 92037-000  
Telephone: (619) 554-8048  
FAX: (619) 554-8841

DATE: June 10-11, 1992

TOPIC: TO BE ANNOUNCED

LOCATION:  
Oklahoma City Marriott  
3233 Northwest Expressway  
Oklahoma City, OK 73112  
Telephone: (405) 842-6633  
FAX: (405) 842-3152

SPONSOR:  
University of Oklahoma Health Sciences Center

REGISTRATION:  
Ms. Marilyn Perry, Assistant to Director for Compliance  
Division of Animal Resources  
BMSB/Room 203  
University of Oklahoma Health Sciences Center  
Telephone: (405) 271-5185  
FAX: (405) 271-3032

#### NOTICES OF AVAILABILITY (RFPs AND RFAs)

#### DEVELOPMENTAL RESEARCH IN NATIVE PACIFIC POPULATIONS

NIH GUIDE, Volume 21, Number 40, November 6, 1992

RFA AVAILABLE: CA-93-06

P.T. 34, FB; K.W. 0715035, 0795003, 0745027

National Cancer Institute

Letter of Intent Receipt Date: December 4, 1992  
Application Receipt Date: January 25, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICATIONS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Cancer Program is mandated to address the unique cancer prevention, early detection, and treatment needs of all populations within the U.S. and its territories. Therefore, the Special Populations Studies Branch (SPSB) of the Division of Cancer Prevention and Control (DCPC) of the National Cancer Institute (NCI) invites applications from various organizations for developmental studies that: (1) assess cancer control need, (2) determine barriers to cancer control, and/or (3) validate intervention methods and assessment instruments in native Pacific populations; i.e., American Samoans, Guamanians (Chamorros), Palauians, and Northern Marianians. This initiative will define the cancer prevention and control needs of native Pacific populations and those of similar ancestry located in the Pacific as well as the U.S. mainland.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Developmental Research in Native Pacific Populations, is related to the priority area of cancer. Potential applicants may obtain a copy of Healthy People 2000 (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000 (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: 202/783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic (including U.S. Territorial possessions) public and private, for-profit and non-profit organizations serving native Pacific populations such as universities, public health departments, voluntary organizations, research centers, hospitals, consortia of health providers, units of State and local governments and eligible agencies of the Federal government. Teams of applicants are encouraged. Among a team of applicants, one institution must be proposed as the lead institution to serve as the applicant and to assume responsibility for the conduct and administration of the project. Note that awards will not be made to foreign institutions and that applications from domestic organizations may not include international components.

The mechanism of support for this RFA will be the National Institutes of Health (NIH) research project grant (R01). Responsibility for the planning, direction, and execution of the proposed research will be solely that of the applicant. In addition to the requirements stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1991. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures. It is anticipated that four awards will be made at approximately \$300,000 total costs per year.

#### FUNDS AVAILABLE

Approximately \$1.2 million in total costs per year for three years will be set-aside to specifically fund applications that are submitted in response to this RFA. It is anticipated that up to four awards will be made. The total project period of these awards may not exceed three years. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI, the award of a grant pursuant to this RFA is also contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

Studies conducted under this RFA will seek to define cancer prevention and control needs/services of the native Pacific population segments (Phase I). Studies to test ways in which existing intervention methods can be used or adapted for the target populations (Phase II); or studies of new methods designed to be sensitive to the needs of the target populations (Phase II); or methodologic research on validation of assessment instruments in target populations (Phase II) are eligible for consideration under the RFA. This "developmental cancer control research" (Phase I and Phase II) is absolutely essential to future development of cancer prevention and control research for native Pacific populations.

The following definitions apply for this RFA:

**Cancer Control** -- Cancer control is defined as the reduction of cancer incidence, morbidity, and mortality through an orderly sequence from research on interventions and their impact in defined populations to the broad, systematic application of the research results.

**Phases of Cancer Control** -- Cancer control research studies are classified in the five phases that represent the orderly progression noted in the above definition: (I) Hypothesis development; (II) Intervention methods development and testing; (III) Controlled intervention trials to establish cause and effect relationships; (IV) Research in defined human populations; and (V) Demonstration and implementation studies.

The research of interest in this RFA falls into either Phase I or Phase II studies. Hypothesis development (Phase I) studies should focus on the assessment of cancer prevention and control needs in communities or organizations within native Pacific populations or studies that identify barriers to cancer prevention and control within these indigenous populations. Methods development and testing studies, Phase II, should focus on: (1) validating the use of existing intervention methods (e.g., dietary modification, health services, tobacco cessation) applied in the target populations described above; (2) developing and pilot testing unique methods that are sensitive to the needs of the target populations described above; or (3) developing and validating assessment instruments to measure the cancer control related needs of the target populations or for use in evaluating the effectiveness of intervention methods in the target populations.

#### STUDY POPULATIONS

The targeted population of this RFA is the native Pacific populations and those of similar ancestry located in the Pacific as well as the U.S. mainland; i.e., American Samoans, Guamanians (Chamorros), Palauians, and North Marianians. Applicants responding to this RFA are expected to successfully access a significant portion of this population to decrease cancer incidence and mortality, increase cancer survival, and increase the diagnosis of cancers at earlier stages.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by December 4, 1992, a letter of intent that includes a descriptive title of the proposed research; the name, address, and telephone number of the Principal Investigator (PI); the identity of other key personnel and participating institutions; and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid possible conflict of interest in the review. The letter of intent is to be sent to Dr. George A. Alexander at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91). These forms are available at most institutional offices of sponsored research and the Office of Grants Inquiries, Division of Research

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed (initially) by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the RFA is an NCI program staff function. If an application is judged to be non-responsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered with other unsolicited applications received by NIH in the next review cycle. Questions concerning responsiveness to the RFA may be directed to NCI program staff identified under INQUIRIES. Those applications that are complete and responsive will be initially evaluated in accordance with the review criteria stated within the RFA for scientific/technical merit by an ad hoc review committee convened by the Division of Extramural Activities, NCI. The second level of review will be provided by the National Cancer Advisory Board.

#### INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome. Direct requests for the RFA and inquiries regarding programmatic issues to:

George A. Alexander, M.D.  
Chief, Special Populations Studies Branch  
Cancer Control Science Program  
Division of Cancer Prevention and Control  
National Cancer Institute  
Executive Plaza North, Room 240  
Bethesda, MD 20892-4200  
Telephone: (301) 496-8589  
FAX: (301) 496-8675

Direct inquiries regarding fiscal issues to:

Crystal Elliott  
Grants Management Specialist  
National Cancer Institute  
Grants Administration Branch  
Executive Plaza South, Room 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800 Ext. 19

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.399, Cancer Control Science Program. Awards are made under authorization of the Public Health Service Act, Title IV, Part A. (Public Law 78-410, as amended by Public Law 99-158, 42 USC 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### NETWORK OF PEDIATRIC PHARMACOLOGY RESEARCH UNITS

NIH GUIDE, Volume 21, Number 40, November 6, 1992

RFA AVAILABLE: HD-93-06

P.T. 34, AA; K.W. 0710100, 0770005, 0403020, 0715006

National Institute of Child Health and Human Development

Letter of Intent Receipt Date: February 15, 1993

Application Receipt Date: April 13, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED BELOW.

#### PURPOSE

The National Institute of Child Health and Human Development (NICHD) will support a cooperative network of Pediatric Pharmacology Research Units (PPRU) to facilitate clinical studies of drug action and disposition in infants and children. These studies are to be conducted by qualified pediatric clinical pharmacologists, either cooperatively with investigators at other Units in the network, collaboratively with pharmaceutical companies, or independently with other support. The major goal of studies conducted by the PPRU Network is to provide the clinical data on drugs necessary for U.S. Food and Drug Administration (FDA) approval for use in children.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention goals of "Healthy People 2000," a PHS-led national activity for setting priorities. This RFA, Network of Pediatric Pharmacology Research Units, is related to the priority areas of food and drug safety and maternal and infant health. Copies of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0, or Summary Report: Stock No. 017-001-00473-1) are available through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).



PPRU cooperative clinical agreement (U10) awards will be made to children's hospitals or the equivalent, or to educational institutions with accredited medical schools, within the United States. The applicant institution must also meet the standard eligibility requirements for research grants established in the Public Health Service Grants Policy Statement # (OASH) 90-50,000, rev. 10/1/90.

There must be at the applicant institution an ongoing program of excellence in clinical pharmacology, with an emphasis on pediatric applications. The quality of this program must be evident from the receipt by its staff of research support in peer-reviewed competition or from their consistent record of publication in peer-reviewed research journals. In addition, the applicant institution must have available a sufficient number of eligible research subjects in the pediatric age groups: newborns, infants, children, pre-adolescents, and adolescents.

#### MECHANISM OF SUPPORT

The funding mechanism to be used to assist the scientific community in undertaking this program of clinical pharmacologic investigation will be a cooperative clinical agreement (U10) between the participating units and the NICHD. The U10 award provides support for laboratory and administrative resources to assist the research community in carrying out clinical therapeutic research. The major difference between a cooperative agreement and a traditional research grant is the substantial scientific involvement of NICHD staff beyond the levels normally required for program stewardship of grants.

#### FUNDS AVAILABLE

It is expected that up to four applications will be funded, within the total direct cost limit of \$1,000,000 available for the first year. Therefore, the maximum direct cost request (first year) for individual applications should not exceed \$250,000. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NICHD, awards pursuant to this RFA are contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

Federal law and the regulations of the FDA require that drugs be tested for safety and efficacy before they are approved for clinical use. This testing must take place with all populations with which the drug will be employed. Studies must therefore be conducted with infants and children before a drug can be approved for use with them.

Several practical problems discourage the testing of drugs and medical devices in children. These include the unpredictable nature of some of the clinical responses; the possibility of catastrophic unanticipated reactions; the threat of adverse effects on growth; the ethical problems of conducting nontherapeutic research in children; and the absence of a financial incentive for pharmaceutical companies when children are a minority of the population for whom the drug might be prescribed. The result of these practical problems and the regulatory requirements is that more than three-quarters of the drugs marketed in the United States, including many of the most useful agents in modern therapy, are not approved as safe and effective for use in children. Since the provision of pediatric care without the use of these agents would be unacceptable, they are often administered "off-label," meaning without specific FDA approval.

This dilemma must be resolved if children are to escape the status of therapeutic orphans and to receive the full benefits of contemporary therapeutics. Modern pediatric pharmacology is a sophisticated clinical discipline capable of carrying out the studies necessary for the safe and ethical evaluation of drugs in children. Pursuit of such studies, however, is limited by the scarcity of available facilities in which to perform them and the small number of qualified clinical investigators interested in this problem.

The objective of the PPRU Program is to increase the number and variety of medications that are FDA-approved for use in children, with the ultimate goal that all drugs prescribed for children be labeled for such usage. This is to be accomplished by providing resources for pediatric pharmacokinetic and pharmacodynamic research through the establishment of a network of pediatric pharmacology research units.

Each PPRU will have four specific aims:

- (1) To participate with other units in the network and with NICHD staff assistance in collaborative clinical trials of drugs in children through protocols determined by consensus;
- (2) To provide a locus for the conduct of pre-marketing and post-marketing clinical trials in children by qualified clinical pharmacologists working in collaboration with proprietary pharmaceutical firms;
- (3) To conduct independent, investigator-initiated studies on the pharmacodynamics and pharmacokinetics of drugs in children; and
- (4) To provide an environment in which pediatricians and others can gain supervised experience in pediatric clinical pharmacology.

The PPRU group will be organized through a Network Steering Committee (NSC), comprising the Principal Investigators (PI) of the funded units, one NICHD staff member, and appropriate outside advisers. This committee will meet at least quarterly to review and select protocols to be performed collaboratively by the network and to exchange information on progress. The NSC will be chaired by a non-NICHD scientist not affiliated with any of the units.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion



of females and minorities in study populations. If minorities are not included in the study populations, a specific justification for this exclusion must be provided. Applications without such inclusion or justification will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by February 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NICHD staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

Ephraim Y. Levin, M.D.  
Endocrinology, Nutrition and Growth Branch  
Center for Research for Mothers and Children  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 637  
Bethesda, MD 20892  
Telephone: (301) 496-5593

#### APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398, and must be received by April 13, 1993. Potential applicants must request the detailed information included in the complete RFA before preparing an application.

#### REVIEW CONSIDERATIONS

Applications will be reviewed by NICHD staff for responsiveness to the RFA. A non-responsive application will be returned to the applicants. Responsive applications may be subjected to a triage by a peer-review group to determine the scientific merit relative to the other applications received in response to this RFA. The NICHD will withdraw from competition those applications judged to be noncompetitive and notify the applicants and institutional business officials.

Applications considered responsive to this RFA will be reviewed for technical merit by an Initial Review Group convened by the scientific review staff of the NICHD solely to evaluate these applications. Criteria for the initial review are described in the RFA. Following review by the Initial Review Group, applications will be evaluated by the National Advisory Child Health and Human Development (NACHHD) Council for program relevance and policy issues before awards are made.

#### INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Ephraim Y. Levin, M.D.  
Endocrinology, Nutrition and Growth Branch  
Center for Research for Mothers and Children  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 637  
Bethesda, MD 20892  
Telephone: (301) 496-5593

Direct inquiries regarding fiscal matters to:

E. Douglas Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 505  
Bethesda, MD 20892  
Telephone: (301) 496-1303

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.865, Research for Mothers and Children. Awards are made under authorization of the Public Health Service Act, Section 301 (42 USC 421), and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Health Systems Agency review.

NIH GUIDE, Volume 21, Number 40, November 6, 1992

RFA AVAILABLE: DK-93-12

P.T. 34; K.W. 0785095, 0755018

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: April 19, 1993

Application Receipt Date: May 18, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

This initiative invites grant applications for biomedical research utilizing the United States Renal Data System (USRDS) database.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Research Using the United States Renal Data System, is related to the priority area of Diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Minority individuals and women are encouraged to submit as Principal Investigators.

#### MECHANISM OF SUPPORT

Support of this program will be through the investigator initiated research project grant (R01) mechanism. Each grant award will not be more than \$50,000 total cost (including direct and indirect costs). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement.

This RFA is a one-time solicitation. Generally, future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures. The total requested project period for each application submitted in response to this RFA may not exceed two years. The earliest possible award date will be January 1994.

#### FUNDS AVAILABLE

It is anticipated that approximately 10 awards will be made. However, this funding level is dependent upon the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the award of grants pursuant to this RFA is also contingent upon the availability of funds designated for this purpose.

#### RESEARCH OBJECTIVES

The USRDS database contains information on 420,000 Medicare patients who have had end-stage renal disease (ESRD) therapy at any time since 1976. For each patient, the database includes information on basic demographics, the primary medical diagnosis that led to renal failure, dialysis records, hospital records, transplant information. In addition, the database contains details on the 2,492 institutions that provide ESRD treatment services. Limited information is available on non-Medicare funded ESRD patients who are treated by the Department of Veterans Affairs (no billing record data or social security information). The USRDS database is supplemented by data from the U.S. Census Bureau.

Specific questions that would be considered responsive to this RFA include but are not limited to the following examples: the relative incidence, prevalence, mortality and survival associated with various comorbid conditions, causes of ESRD, modes of ESRD treatment, or subgroups of the treated ESRD population in the United States; examination of the relative burden of disease in various minority groups; ecologic analyses which relate prevalence of predisposing diseases to incidence and prevalence of treated and untreated ESRD in various subgroups of the population. Creativity in using the data to develop descriptive, analytic, and hypothesis generating studies is encouraged. Questions primarily of an economic focus would not be considered responsive to this RFA, although such issues may be included as secondary aims.

The investigator is encouraged to contact the USRDS Project Officer, Dr. Lawrence Agodoa, (KUH/NIDDK, Westwood Building, Room 3A-06, 5333 Westbard Avenue, Bethesda, Maryland 20892, telephone 301/496-7571), to discuss the data request and to request a copy of the USRDS Data Release Policy and the USRDS Agreement for Data Release Form. The USRDS database may be contacted at any time. The USRDS process of reviewing a written request for data, generating the data, and releasing the data takes approximately three months.

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by April 19, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDDK staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083

#### APPLICATION PROCEDURES

Applications are to be submitted using form PHS 398 (rev. 9/91), available in most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441. The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page. Detailed instructions on submission procedures are described in the RFA.

#### REVIEW CONSIDERATIONS

Applications that are complete and responsive to the RFA will be evaluated by an appropriate peer review group convened by the NIDDK in accordance with the usual NIH peer review procedures. Following initial review, the applications will be given a secondary review unless not recommended for further consideration by the initial review group. Applications that are incomplete or unresponsive to the RFA will be returned to the applicant or held until the next regular receipt date and reviewed by the Division of Research Grants. Review criteria are given in the RFA.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. Inquiries regarding programmatic issues, and requests for the RFA may be directed to:

Camille A. Jones, M.D., M.P.H.  
Director, Epidemiology Program  
Division of Kidney, Urologic, and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A-06  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7571

Inquiries regarding fiscal matters may be directed to:

Ms. Trude McCain  
Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
5333 Westbard Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.849. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

THE IMMUNOLOGY OF AGING

NIH GUIDE, Volume 21, Number 40, November 6, 1992

PA NUMBER: PA-93-014

P.T. 34; K.W. 0710010, 0710070, 0705040, 0765035

National Institute on Aging  
National Institute of Allergy and Infectious Diseases

## PURPOSE

It has been well established that overall immune function declines with advancing age. However, because the immune system is highly complex, it is essential to understand the multi-faceted nature of this age-related loss of immune function and to identify the primary changes in immune mechanisms leading to this decline in the immune responses. It has been proposed that the decline and/or dysregulation of the immune system may be a primary cause of aging or perhaps a pace-setter of the aging process. The possibility that changes in the immune system may be a fundamental predisposing factor in the aging process is also an appropriate field of scientific inquiry. Research is also indicated into the pathological consequences of age-related changes in the immune system, such as decreased resistance to infection with pathogens and an increased tendency toward autoimmunity and immunopathology.

The Biology of Aging Program (BAP) of the National Institute on Aging (NIA) has responsibility for supporting extramural research and training in the fundamental studies of immunology as related to aging. The Geriatrics Program (GP) has responsibility for supporting clinical studies of the immune competence of aging humans, the transfer of promising immunological interventions, and the delivery of effective vaccines to geriatric populations. The Division of Allergy, Immunology, and Transplantation (DAIT) of the National Institute of Allergy and Infectious Diseases (NIAID) is responsible for promoting research into the basic mechanisms of the immune system and the changes that occur in the immune system that initiate or contribute to disease. The two institutes share the goal of achieving a better understanding of the behavior of the immune system and the specific deficits of various components of the immune system that occur during aging to permit intervention and prevent or reverse the immunologic deficits of aging.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Applicants for K and F awards must be U.S. citizens, non citizen nationals, or have been lawfully admitted for permanent residence at the time of award. Applications related to the health of women and minorities are particularly encouraged.

## MECHANISMS OF SUPPORT

- o Research grant (R01)
- o Program Project grant (P01)
- o First Independent Research Support and Transition (FIRST) award (R29)
- o Career grants, which include: Research Career Development Award (K04); Clinical Investigator Award (K08); Physician Scientist Award (individual K11)
- o Training grants (T32)
- o Fellowships (F32, F33)

Deadlines for applications are as follows:

F-series and T-series grants:	Jan 10, May 10, Sep 10
New R, K, and P-series:	Feb 1, Jun 1, Oct 1
Competing continuation and revised:	Mar 1, Jul 1, Nov 1

Foreign institutions are not eligible to apply for T32 Awards, Program Project (P01) Awards, or FIRST Awards (R29).

## RESEARCH OBJECTIVES

The NIA and the NIAID invite investigators to submit applications for research and research training in all areas of immunology that relate to fundamental processes of aging. Applications to study the aging of the immune system in humans, animals, or cell culture systems are welcome. Applications that might lead to successful interventions in the aging of the immune system are particularly encouraged.

The following topics are illustrative of appropriate research areas covered by this Program Announcement. However, applications need not be limited to the issues listed below.

- o Age related changes in the functions of lymphoid organs (thymus, spleen, lymph nodes, gut-associated lymphoid tissue)



- o The roles of changes in bone marrow cell production and thymic involution in the aging immune response. The possible role, source and mechanism of extrathymic T cell repopulation
- o Age-related changes in the genetic and ontogenic control of T and B cell production. Selection and deletion of involved cell types. The nature and function of different T and B cell subtypes (naïve, memory, helper, and cytotoxic T cells)
- o Age-related changes in the mechanisms of antigen sequestration, transport, processing, and presentation, including the accessory cells involved (Langerhans cells, macrophages, dendritic cells, B cells)
- o Age-related changes in molecules involved in specific antigen recognition (B-cell and T-cell receptors, MHC-encoded molecules) and in lymphocyte and macrophage activation
- o Age-related changes in biochemical processes leading to lymphocyte and macrophage activation
- o Age-related changes in the production of lymphokines and other cytokines (and their receptors) involved in the immune response
- o The role of hormones and neuroendocrine factors in the regulation of T and B cell activity and in age-related changes in immune function.
- o Age-related changes in the regulation of the immune response (e.g., regulatory cells, immunoglobulin isotypes, the idiotypic network). Changes in the nature of the antibody repertoire with aging.
- o Immune responses to infectious agents and to vaccines in senescence; development of vaccine delivery systems.
- o Immunologic tolerance, autoimmunity, and immunopathology in senescence
- o The interrelationship between disease and immune function in the aging process
- o The role of nutrition and caloric restriction in the potentiation or prevention of age-associated deficits in immune function
- o Immune surveillance in aged individuals
- o Generalized immunosuppression due to viral, protozoal, and bacterial infections in aged individuals
- o Attempts to prevent or reverse the immunologic deficits of aging by immunotherapy (e.g., development of techniques for immune augmentation, biological response modifiers, hormonal treatment)
- o Attempts to prevent or reverse the immunologic deficits of aging through cellular or genetic engineering
- o Effects of drugs on the immune system of older individuals
- o Gender-related differences in any of the above areas of research.

The Geriatrics Program of the NIA also supports research in the clinical aspects of several of the preceding topics, particularly those regarding immune responses to infectious agents in senescence and the development and delivery of effective vaccines. Inquiries considered more appropriate for the Geriatrics Program will be referred to them.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 3, Recruitment of Individuals from Underrepresented Racial/Ethnic Groups, and Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in ALL research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should

be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities. If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions. National Research Service Award (NRSA) (F32, F33) applications must be submitted on grant application Form PHS 416 (rev. 10/91).

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

Applications from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator could be included with the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Other institutes may also have interest in several of the topics mentioned here. All applications in response to this Program Announcement will be assigned to an Initial Review Group and reviewed by the usual Public Health Service Peer Review (Study Section) procedures. They will also be given appropriate primary and secondary Institute assignments in accordance with established PHS Referral Guidelines. The review criteria are the traditional criteria appropriate to each mechanism. In accordance with the standard NIH peer review procedures, research project grant (R01 and R29) applications, fellowships (F32, F33) and research career development awards (K04) will be reviewed for scientific and technical merit by an appropriate study section in the Division of Research Grants. All other applications will be reviewed by review groups of the appropriate funding component. Following the Study Section review, the applications will receive a second-level review by the appropriate advisory council. Funding decisions will be based on the above evaluations and on the availability of funds.

#### AWARD CRITERIA

Applications compete for available funds on the basis of scientific merit. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Researchers considering an application in response to this announcement are strongly encouraged to discuss their project, and the range of grant mechanisms available with NIA and/or NIAID staff. This can be done either through a telephone conversation or a brief letter.

Correspondence and inquiries may be directed to:

Dr. David Lavrin, Immunology Program Administrator  
Biology of Aging Program  
National Institute on Aging  
Gateway Building, Room 2C231  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-6402  
FAX: (301) 402-0010

Dr. Joseph Albright  
Program Administrator, Division of Allergy, Immunology and Transplantation  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4A20  
Bethesda, MD 20892  
Telephone: (301) 496-7985  
FAX: (301) 402-0175

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.866 and 93.855. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### PHYSIOLOGICAL ROLE OF THE ADRENAL ANDROGEN, DHEA, IN AGING

NIH GUIDE, Volume 21, Number 40, November 6, 1992

PA NUMBER: PA-93-015

P.T. 34; K.W. 0710010, 0705030, 0705040, 0760025

National Institute On Aging

#### PURPOSE

The National Institute on Aging (NIA) has responsibility for extramural programs of research and training in immunology and endocrinology related to aging. This support has resulted in a better understanding of the behavior of, and specific changes in, various components of the immune and endocrine systems in aging.

It is well recognized that changes in the immune and endocrine systems during aging have profound influences on homeostatic mechanisms of the body. Some of these changes may be a result of "normal aging;" others may be due to environmental factors, such as stress and disease. Steroid, peptide, and eicosenoid hormones secreted from endocrine tissues are known to influence the immune system. Conversely, some cytokines, interferons and interleukins, modulators of immune system function, have profound regulatory effects on the endocrine system. Since both the immune and some components of the endocrine systems decline with advancing age, it is of interest to explore and delineate regulatory interactions between the immune and endocrine systems in the aging mammal.

The purpose of this program announcement is to focus on the physiological role of the adrenal steroidal androgen precursor, dehydroepiandrosterone (DHEA), in aging. DHEA, and its sulfated form, DHEAS, decrease steadily with age in both animals and humans. This decline may represent a biomarker of biological aging. DHEA/DHEAS levels have also been found to be depressed in a number of disease states (eg., systemic lupus erythematosus (SLE), AIDS, cancer, diabetes, cardiovascular disease) and during stress and trauma (e.g., burns, surgery). Administration of DHEA has been shown to inhibit the development of obesity and to protect against carcinogenesis in mice. Recent research has demonstrated that the administration of physiologic doses of DHEA/DHEAS to aged mice may reverse the age-related immunological anergy by permitting the production of antibody and cellular responses at levels comparable to those of fully immunocompetent mature adult mice. The pattern of the lymphokine production was also restored to that of normal mature mice. DHEAS administration also has been shown to counteract the inflammatory production of Interleukin-6 and the effects of corticosteroids following stress and trauma.

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Applicants for K- and F-series awards must be U.S. citizens, non-citizen nationals, or have been lawfully admitted for permanent residence at the time of award.

#### MECHANISMS OF SUPPORT

- o Research grant (R01)
- o Program Project grant (P01)
- o First Independent Research Support and Transition (FIRST) award (R29)
- o Career grants, which include: Research Career Development Award (K04); Clinical Investigator Award (K08); Physician Scientist Award (individual K11)
- o Fellowships (F32, F33)

Deadlines for applications are as follows:

F-series grants:	Jan 10, May 10, Sep 10
New R, K, and P-series:	Feb 1, Jun 1, Oct 1
Competing continuation and revised:	Mar 1, Jul 1, Nov 1

Foreign institutions are not eligible to apply for Program Project (P01) awards, or FIRST awards (R29).



## RESEARCH OBJECTIVES

The NIA invites researchers to submit applications for research grants, career development awards, and postdoctoral fellowships for studies on the role of DHEA/DHEAS and their metabolic products as they interface with fundamental aging. Of particular interest is the pathway of action and its possible role as a biomarker of aging, including the decline of the immune system and the propensity for increased disease in aging. Of interest also are potential intervention methods to delay and control the aging process with respect to the susceptibility to diseases of the immune, endocrine, and other physiologic systems.

Although the interaction of DHEA/DHEAS and their metabolic products and analogs with components of the immune system and various pathophysiologic processes is of primary interest in this Program Announcement, other relevant areas of investigation exploring the communication between the immune and endocrine systems in aging mammals are also of interest and are included within the scope of this Program Announcement.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 3, Recruitment of Individuals from Underrepresented Racial/Ethnic Groups, and Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in ALL research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

## APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions. National Research Service Award (NRSA) (F32, F33) applications are to be submitted on grant application Form PHS 416 (rev. 10/91).

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of this announcement must be typed in Section 2a on the face page of the application.

Applications from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator could be included with the application.



The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

All applications in response to this Program Announcement will be assigned to Initial Review Groups on the basis of the PHS Referral Guidelines and reviewed by the usual Public Health Service Peer Review (Study Section) procedures. They will also be given appropriate primary and secondary Institute assignments in accordance with established PHS Referral Guidelines. The review criteria are the traditional criteria appropriate to each mechanism. In accordance with the standard NIH peer review procedures, research project grant (R01 and R29) applications, fellowships (F32, F33) and research career development awards (K04) will be reviewed for scientific and technical merit by appropriate study sections in the Division of Research Grants. All other applications will be reviewed by review groups of the appropriate Institute. Following the Study Section review, the applications will receive a second-level review by appropriate advisory councils. Funding decisions will be based on the above evaluations and on the availability of funds.

#### AWARD CRITERIA

Applications compete for available funds on the basis of scientific merit with other applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Researchers considering an application in response to this announcement are strongly encouraged to discuss the projects and the range of grant mechanisms available, with NIA staff. This can be done either through a telephone conversation or a brief letter. Applications related to the health of women and minorities are particularly encouraged.

Correspondence and inquiries may be directed to:

Dr. David Lavrin  
Immunology Program Administrator  
Biology of Aging Program  
National Institute on Aging  
Gateway Building, Room 2C231  
Bethesda, MD 20892  
Telephone: (301) 496-6402

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.855. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816



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# NIH GUIDE

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## For Grants and Contracts

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**Building 31, Bethesda, Maryland 20892**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

**Vol. 21., No. 41, Part I of II**  
**November 13, 1992**

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National Institutes of Health





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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

# NOTICES

## NATIONAL HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 41, November 13, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to

all other Public Health Service agencies. The current schedule includes the following:

#### SOUTHWESTERN WORKSHOP

DATES: November 16 & 17, 1992

#### LOCATION:

Wyndham Warwick  
5701 Main Street  
Houston, TX 77005  
Telephone: (713) 526-1991

#### SPONSORS:

University of Texas Health Science Center at Houston  
Prairie View A&M University

#### REGISTRATION:

Ms. Paula Knudson  
Executive Coordinator  
Office of Research Support Committee  
University of Texas Health Science Center at Houston  
P.O. Box 20036  
Houston, TX 77225  
Telephone: (713) 792-5048

TITLE: Geriatric Research as an Ethical Mandate: Politics, Policy, and Problems

DESCRIPTION: Expanded life expectancies and expanding technologies are swelling the ranks of the frail and disabled elderly. Minimal research has been carried out to understand the problems this subject group and their families encounter in finding solutions to their health and social needs. The conference will identify key problems that need to be studied; isolate the risks and benefits associated with behavioral, clinical, or evaluation research designed to enroll this group as subjects; and pose solutions that will meet the needs of regulators, scientists, and the elderly.

The program is designed to be of interest to physicians, nurses, pharmacists, scientific investigators, and other health care professionals, clergy, lawyers, medical, nursing, social work students, psychologists, and IRB members and administrators. Attention will be paid to Federal regulations with special emphasis on the assessment of risks---medical, legal, and psychosocial. Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR and FDA representatives.

#### SOUTHEASTERN WORKSHOP

DATES: January 14 & 15, 1993

#### LOCATION:

Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

#### SPONSORS:

University of South Florida  
Florida A & M University

#### REGISTRATION:

Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.

The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

For further information regarding these workshop and future NIH/FDA National Human Subject Protections

Workshops, please contact:

Ms. Darlene Marie Ross  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

NOTICES OF AVAILABILITY (RFPs AND RFAs)

LABORATORY FOR ASSESSMENT OF MUCOSAL IMMUNE RESPONSES INDUCED BY AIDS VACCINES IN CLINICAL TRIAL VOLUNTEERS

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFP AVAILABLE: NIAID-DAIDS-93-18

P.T. 34; K.W. 0715008, 0740075, 0755010, 0710070

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID), NIH, has a requirement to provide for the centralized performance of immunological assays to evaluate HIV-specific humoral and cellular mucosal immune responses in support of clinical trials of prototype AIDS vaccines. The purpose of this contract is to support the NIAID in its mission to stimulate research towards discovery and testing of prototype vaccines for the acquired immunodeficiency syndrome (AIDS). The NIAID requires a Mucosal Immunology Laboratory to evaluate reproductive tract, gut, blood, and other mucosal specimens from vaccine clinical trial volunteers for humoral and cellular mucosal immune responses induced by immunization with prototype AIDS vaccines. This effort will support the research of AIDS investigators, including the AIDS Vaccine Evaluation Group (AVEG), the National Cooperative Vaccine Evaluation Groups (NCVDG), and other programs initiated by NIAID.

Specifically, the selected Contractor shall be responsible for: (1) performing specific immunological assays for detection of HIV-specific antibody and cellular responses in mucosal site and blood specimens from AIDS vaccine recipients; (2) developing standard protocols for the collection, processing, and storage of mucosal specimens at the vaccine trial sites; (3) receiving, cataloging, tracking, coding, storing, and maintaining an inventory of vaccinee specimens arriving for evaluation; and (4) maintaining a test result database and transferring data electronically to the AIDS Vaccine Clinical Trials Network (AVCTN) Data Coordinating and Analysis Center (DCAC).

This is an announcement for an anticipated Request for Proposals (RFP). RFP: NIH-NIAID-DAIDS-93-18 will be issued on or about November 13, 1992 with a closing date tentatively set for January 5, 1993. It is expected that one (1) contract will be awarded as a result of this solicitation. It is expected that the contract will have a five-year period of performance, and a completion type cost-reimbursement contract is anticipated.

INQUIRIES

Requests for the RFP may be directed in writing to:

Lawrence Butler, Contracting Officer  
Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C-07  
6003 Executive Boulevard  
Bethesda, MD 20892

Please provide this office with three self-addressed mailing labels. Telephone inquiries will not be honored and all inquiries must be in writing. A short-form version of the RFP will be provided first, which includes only the statement of work and the Evaluation Criteria to be used for selection of the awardee.

After examining this, a full-text version of the RFP must be requested in writing by those offerors interested in responding. FAX requests are acceptable for the full-text version of the RFP only (FAX: 301-402-0972). All proposals from responsible sources will be considered by the NIAID. This advertisement does not commit the Government to award a contract.

BIOCHEMICAL SCREENS FOR AGENTS EFFECTIVE AGAINST AIDS-RELATED OPPORTUNISTIC INFECTION

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFP: NIAID-DAIDS-93-19

P.T. 34; K.W. 0755010, 0715008, 0755060, 0760013

National Institute of Allergy and Infectious Diseases

The Developmental Therapeutics Branch, Basic Research and Development Program, Division of AIDS, National Institute of Allergy and Infectious Disease (NIAID), NIH has a requirement to apply established biochemically-based enzymatic or non-enzymatic assays to screen agents for inhibition of one or more steps in

the metabolism of AIDS-associated opportunistic pathogens. These biochemical prescreens are considered particularly useful for rapid testing of compounds. Examples of such assays may include, but not be limited to: protein synthesis, dihydrofolate reductase, and dihydropteroate synthase. The major effort of this contract will involve the screening of a large number of compounds. A secondary focus of this contract will be development/modification of automated biochemical assays and their application to drug testing against opportunistic infections in AIDS. It is anticipated that some assays will require isolation of enzymes from relevant microorganisms or cloning to obtain the protein. However, most of the enzymes and recombinant proteins required for the development of assays in this project will be provided by the AIDS Reference and Reagent Repository. Other non-enzymatic assays may be developed /used to evaluate drug activities in vitro. At the present time, NIAID has one contract that is scheduled to end in 1993 to screen agents in enzymatic assays.

This NIAID sponsored project will take approximately three years to complete. A level-of-effort, cost reimbursement contract is anticipated. It is expected that one award will be made.

This is an announcement for an anticipated Request for Proposal (RFP). RFP NIH-NIAID-DAIDS-93-19 will be issued on or about November 12, 1992, with a closing date tentatively set for January 15, 1993.

#### INQUIRIES

Requests for the RFP may be directed in writing to:

Cyndie Cotter  
Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C07  
6003 Executive Boulevard  
Bethesda, MD 20892

To receive a copy of the RFP, please supply this office with three self-addressed mailing labels. Telephone inquiries will not be honored and all inquiries must be in writing. A short-form version of the RFP will be provided first, which includes only the Statement of Work and the Evaluation Criteria to be used for selection of the awardee. After examining this, a full-text version of the RFP must be requested, in writing, for those offerors interested in responding. FAX requests are acceptable for the full-text version only (FAX: 301-402-0972). All proposals from responsible sources will be considered by the NIAID. This advertisement does not commit the Government to award a contract.

#### GENETIC SEQUENCE VARIABILITY OF HIV-1 AND RELATED LENTIVIRUSES

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFP: NIH-NIAID-DAIDS-93-22

P.T. 34; K.W. 1215018, 0755018

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID), NIH, has a requirement for a contractor to receive samples infected with HIV-1 or related lentiviruses, to amplify virus-specific genetic sequences from these samples, and to clone and sequence these amplified fragments. The Contractor will be required to design gene amplification primers for distinct regions of the virus genome and for diverse viral isolates. The Contractor will be required to amplify and clone sizable genomic fragments (>1500 base pairs), and carry out large-scale genetic sequencing (approximately 200,000 bases/year).

Specifically, the selected contractor shall be responsible for: (1) amplifying, cloning and sequencing HIV-1 and related lentivirus-specific gene fragments from samples derived from HIV-infected individuals provided through the Project Officer; (2) compiling and analyzing genetic sequence data, and transferring data to the HIV Genetic Sequence Database and Analysis Unit at the Los Alamos National Laboratory; (3) receiving, cataloging, processing, storing samples, and distributing samples to other investigators; and (4) providing an Inventory and Database Management System.

This is an announcement for an anticipated Request for Proposals (RFP). RFP NIH-NIAID-DAIDS-93-22 will be issued on or about November 9, 1992, with a closing date tentatively set for January 5, 1993. One contract will be awarded as a result of this solicitation. It is expected that the contract will have a five-year period of performance. A level-of-effort cost-reimbursement contract is anticipated.

#### INQUIRIES

Requests for the RFP are to be directed in writing to:

Kristiane E. Hofacker, Contract Specialist  
Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C07  
Bethesda, MD 20892

Please provide this office with three self-addressed mailing labels. Telephone inquiries will not be honored and all inquiries must be in writing. A short-form version of the RFP will be provided first, this includes only the Statement of Work and the Evaluation Criteria to be used for selection of the awardee. After examining this, a full-text version of the RFP must be requested, in writing, for those offerors interested in responding. FAX requests are acceptable for full-text versions of the RFP only (FAX: 301/402-0972). All proposals from



responsible sources will be considered by the NIAID. This advertisement does not commit the Government to award a contract.

#### CLINICAL TRIALS CENTER FOR ANTIHYPERTENSIVE AND LIPID-LOWERING TREATMENT TO PREVENT HEART ATTACK TRIAL

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFP AVAILABLE: NHLBI-HC-93-44

P.T. 34; K.W. 0715115, 0755015, 0740025

National Heart, Lung, and Blood Institute

The primary purpose of this program is to select a Clinical Trials Center to conduct a practice-based, randomized clinical trial of antihypertensive pharmacologic treatment and, in a specific subset, lipid-lowering, in a factorial design. The purpose of the antihypertensive trial is to determine whether or not the combined incidence of fatal coronary heart disease (CHD) and non-fatal myocardial infarction differs between diuretic-based and alternative antihypertensive pharmacologic treatment in patients broadly representative of the U.S. hypertensive population, including at least 55 percent African-Americans. The purpose of the lipid-lowering trial is to conduct, in a subset of this population and in a factorial design, a placebo-controlled randomized clinical trial to determine whether or not lowering serum cholesterol in older, moderately hypercholesterolemic men and women with a 3-hydroxymethylglutaryl coenzyme A (HMG CoA) reductase inhibitor will reduce the combined incidence of fatal CHD and non-fatal myocardial infarction. Rather than using independently funded clinics, patients will be recruited through office-based practices and hypertension clinics that will be reimbursed by the Clinical Trials Center on a per-patient basis. The study will consist of a vanguard phase and a full-scale trial phase. Six hundred patients will be entered into the vanguard phase; approximately 30,000 patients will be enrolled in the full-scale trial.

This is not a Request for Proposals (RFP). RFP NHLBI-HC-93-44 will be released on or about November 6, 1992 with proposals due on or about January 15, 1993. One incrementally funded contract is anticipated to be awarded for nine years. Written requests must include three self-addressed mailing labels and must cite RFP NHLBI-HC-93-44.

Requests for copies of the RFP are to be sent to:

Kristee M. Camilletti, Contracting Officer  
HLVD Contracts Section, Contracts Operations Branch, DEA  
National Heart, Lung, and Blood Institute  
Federal Building, Room 4C04  
Bethesda, MD 20892

#### TUBERCULOSIS ACADEMIC AWARD

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFA AVAILABLE: HL-93-09-L

P.T. 34; K.W. 0715165, 0502024, 0785035

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: December 15, 1992  
Application Receipt Date: February 17, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The primary objective of this program is to stimulate the development and/or improvement of the quality of medical curricula, physician/patient and community education, and clinical practice for the prevention, management, and control of Mycobacterial tuberculosis (TB) in the United States.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Tuberculosis Academic Award, is related to the priority areas of immunization and infectious diseases and HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017- 001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

##### Institutions

Applications may be submitted by domestic universities or schools of medicine. Minority institutions and urban institutions from areas with high rates of incidence of TB that have the necessary resources and facilities and a commitment to providing the awardee with the time to develop and implement plans consistent with the goals

of this announcement are encouraged to sponsor candidates for these awards.

#### Candidates

A candidate for an award must:

- o be an established physician and a medical faculty member in an accredited school of medicine or osteopathy in the United States, its territories or possessions, and have competence in tuberculosis and;
- o be employed by a school of medicine or osteopathy that is located in an area with high TB rates;
- o have sufficient clinical training, research, and teaching experience in the control of TB to develop and implement a high quality curriculum in TB encompassing current knowledge and methods applicable to the control of tuberculosis in individuals of all ages and to provide leadership in research in control of TB;
- o be a citizen or non-citizen national of the United States or have been lawfully admitted to the United States for permanent residence at the time of application;

Individuals who have held another NIH career development award (K series) are eligible to apply for the Tuberculosis Academic Award. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA is part of the Academic Award Program (K07) of the National Heart, Lung, and Blood Institute (NHLBI). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period may not exceed five years and is non-renewable. It is anticipated that support for this program will begin September 1993.

#### FUNDS AVAILABLE

The estimated funds (total costs) for the first year of support for the entire program will be \$300,000. It is anticipated that three to four grants will be awarded each year for five years under this program. The specific number, however, will depend upon the merit and scope of the applications received and the availability of funds.

A maximum of \$50,000 for the salary of the awardee, plus applicable fringe benefits, a maximum of \$20,000 for technical support, and indirect costs not to exceed eight percent may be requested.

#### OBJECTIVES

The objectives of the Tuberculosis Academic Award are to:

- o encourage the development of high quality curricula in schools of medicine that will significantly increase the opportunities for students, house staff, and others, including practicing physicians, to learn the principles and practice of preventing, managing, and controlling TB;
- o encourage research in the control of TB;
- o encourage the development of a faculty capable of providing appropriate instruction in TB;
- o contribute to updating the knowledge and skill of practicing physicians and other health care providers in the community;
- o enhance awareness of health care providers of the unique ethnic, cultural, socioeconomic, and medical dimensions of TB;
- o coordinate and collaborate with other community organizations to control TB in areas with high incidence of TB;
- o facilitate an interchange of ideas and methods among awardees and institutions;
- o cooperate and collaborate with other organizations that have responsibility for and interest in TB control, for example, health departments, medical and nursing associations, and voluntary health agencies; and
- o contribute to public health efforts to control TB in the community.

Of particular interest are programs targeted to inner city populations and to rural areas that may be in need of education about TB and among physicians who are or who will be caring for medically underserved populations.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by December 15, 1992, a letter of intent that includes the name,

address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows the Institute staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

C. James Scheirer, Ph.D.  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 548B  
Bethesda, MD 20892  
Telephone: (301) 496-7363

#### APPLICATION PROCEDURES

Applications must be received by February 17, 1993.

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91). Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

#### REVIEW CONSIDERATIONS

Applications for this Tuberculosis Academic Award will be evaluated in terms of the following criteria:

- o the overall merit of the proposed five-year plan for improving the institution's interdepartmental curricula on tuberculosis;
- o the qualifications and background of the candidate, including experience in teaching, curriculum development, and research;
- o the institution's commitment to implement the proposed curriculum and to continue a program in education about tuberculosis control after the termination of the award;
- o the involvement of appropriate disciplines in the development, implementation, and evaluation of the program;
- o design and evaluation plans for educational interventions for health care providers and for patients with tuberculosis, especially in areas with high incidence of TB;
- o plans for communication and cooperation between specialists in adult and pediatric pulmonary medicine, infections, and community medicine to ensure optimal treatment;
- o plans for collaborative projects with other organizations that have responsibility for and interest in tuberculosis control, for example, health departments, medical and nursing associations, and voluntary health agencies;
- o the potential of the program for making an impact on the control of tuberculosis among populations served;
- o the potential for replication or adaptation of the program at other sites.

Of particular interest are programs targeted to inner city populations and to rural areas that may be in need of education about TB and among physicians who are or who will be caring for medically underserved populations.

#### INQUIRIES

Guidelines for this RFA are available from the person named below. Written and telephone inquiries concerning this announcement are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Joan M. Wolle, Ph.D., M.P.H.  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 640  
Bethesda, MD 20892  
Telephone: (301) 496-7668

Direct inquiries regarding fiscal matters to:

Raymond L. Zimmerman  
Grants Operations Branch  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A17  
Bethesda, MD 20892  
Telephone: (301) 496-4970

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.838. Grants will be awarded under the authorization of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended by Public Law 99-158, 42 US 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CAR 52 and 45 CAR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or to a review by a Health Systems Agency.

## ASTHMA ACADEMIC AWARD

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFA AVAILABLE: HL-93-10-L

P.T. 34; K.W. 0715013, 0502024, 0785035

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: December 15, 1992

Application Receipt Date: February 17, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The primary objective of this RFA is to stimulate the development and/or improvement of the quality of curricula, physician/patient and community education, and clinical practice for the prevention, management, and control of asthma in the United States.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Asthma Academic Award, is related to the priority areas of diabetes and chronic disabling diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone: 202-783-3238).

## ELIGIBILITY REQUIREMENTS

### Institutions

Applications may be submitted by domestic universities or schools of medicine. Minority institutions and urban institutions from areas with high rates of morbidity of asthma that have the necessary resources and facilities and a commitment to providing the awardee with the time to develop and implement plans consistent with the goals of this announcement are encouraged to sponsor candidates for these awards.

### Candidates

A candidate for an award must:

- o be an established physician and medical faculty member in an accredited school of medicine or osteopathy in the United States, its territories or possessions, and have competence in the management of asthma, and;
- o be employed by a school of medicine or osteopathy that is located in an area with high asthma morbidity, such as an institution located in an inner city;
- o have sufficient clinical training, research, and teaching experience in pulmonary medicine to develop and implement a high quality curriculum in asthma encompassing current knowledge and methods applicable to the control of asthma in individuals of all ages and to provide leadership in applied research in control of asthma;
- o be a citizen or non-citizen national of the United States or have been lawfully admitted to the United States for permanent residence at the time of application;

Individuals who have held another NIH career development award (K series) are eligible to apply for the Asthma Academic Award. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

This RFA is part of the Academic Award Program (K07) of the National Heart, Lung, and Blood Institute (NHLBI). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period may not exceed five years and is non-renewable. It is anticipated that support for this program will begin September 1993.

A maximum of \$50,000 for the salary of the awardee, plus applicable fringe benefits, a maximum of \$20,000 for technical support, and indirect costs not to exceed eight percent may be requested.



## FUNDS AVAILABLE

The estimated funds (total costs) for the first year of support for the entire program will be \$300,000. It is anticipated that three to four grants will be awarded each year for five years under this program. The specific number, however, will depend upon the merit and scope of the applications received and the availability of funds.

## OBJECTIVES

The objectives of the Asthma Academic Award are:

- o to encourage the development of high quality curricula in schools of medicine that will significantly increase the opportunities for students, house staff, and others to learn the principles and practice of preventing, managing, and controlling asthma;
- o to develop and implement interdepartmental programs with common goals and standardize diagnostic and therapeutic approaches;
- o to promote communication among specialists in primary care, allergy, and obstetrics and gynecology to ensure appropriate treatment of pregnant women with asthma;
- o to encourage research in the control of asthma;
- o to promote the development of a faculty capable of providing appropriate instruction in asthma;
- o to promote an institutional environment that facilitates an interchange of information and educational evaluation techniques about new diagnostic, therapeutic and prevention measures in asthma in both children and adult populations;
- o to investigate coordinated clinical approaches to the care of patients of various ages and ethnic groups who have asthma, such as minorities, young children, and the elderly;
- o to provide for outreach programs from medical centers to health practitioners in the community to enhance optimal care, especially in areas of high asthma morbidity, such as inner city minority communities;
- o to facilitate an interchange of ideas among awardees and institutions;
- o to contribute to public health efforts to control asthma in the United States.

Of particular interest are programs targeted to inner city populations and to rural areas that may be in need of education about asthma and among physicians who are or who will be caring for medically underserved populations.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by December 15, 1992, a letter of intent that includes the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows the Institute staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

C. James Scheirer, Ph.D.  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 548B  
Bethesda, MD 20892  
Telephone: (301) 496-7383

## APPLICATION PROCEDURES

Applications must be received by February 17, 1993.

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91). Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

## REVIEW CONSIDERATIONS

Applications for this Asthma Academic Award will be evaluated in terms of the following criteria:

- o the overall merit of the proposed five-year plan for improving the institution's interdepartmental curricula in asthma control;
- o the qualifications and background of the candidate, including experience in teaching, curriculum development, and research;
- o the institution's commitment to implement the proposed curriculum and to continue a program in education about asthma control after the termination of the award;
- o the involvement of appropriate disciplines in the development, implementation, and evaluation of the program;
- o design and evaluation plans for educational interventions for health care providers and for patients with asthma, especially in areas with high morbidity from asthma, such as inner city minority communities;
- o plans for communication and cooperation between specialists in adult and pediatric pulmonary medicine, family practice, internal medicine, community medicine, and other specialties;
- o plans for collaborative projects with other organizations that have responsibility for and interest in asthma control, for example, health departments, medical and nursing associations, and voluntary health agencies;
- o the potential of the program for making an impact on the control of asthma among populations served;
- o the potential for replication or adaptation of the program at other sites.

## INQUIRIES

Guidelines for this RFA are available from the person named below. Written and telephone inquiries concerning this announcement are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Joan M. Wolle, Ph.D., M.P.H.  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 640  
Bethesda, MD 20892  
Telephone: (301) 496-7668

Direct inquiries regarding fiscal matters to:

Raymond L. Zimmerman  
Grants Operations Branch  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A17  
Bethesda, MD 20892  
Telephone: (301) 496-4970

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.838. Grants are made under the authorization of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended by Public Law 99-158, 42 US 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CAR 52 and 45 CAR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## WOMEN'S INTERAGENCY HIV STUDY

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFA AVAILABLE: AI-92-12

P.T. 34, II; K.W. 0715008, 0740075, 0411005, 0403004, 0785035

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 11, 1993  
Application Receipt Date: February 18, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The Vaccine Trials and Epidemiology Branch (VTEB) of the Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID) invites applications for cooperative agreements for the establishment

of a Women's Interagency HIV Study (WIHS) to investigate the clinical, laboratory, and psychosocial impact of human immunodeficiency virus (HIV) infection in women. The WIHS will use a multi-site, prospective study design to gather data on the clinical, immunological, virological, and behavioral aspects of HIV infection and disease in women. This study will investigate the full spectrum of clinical disease caused by HIV infection in women. It also will seek to determine other cofactors that may be associated with HIV disease progression in women.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, for the Women's Interagency HIV Study, is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-10473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic non-profit, and for-profit research institutions; public and private organizations such as universities, colleges, hospitals or laboratories; units of State and local governments; and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

Applicants must demonstrate the capability to recruit and maintain a minimum of 300 HIV-seropositive women and 75 HIV-seronegative women who engage in activities that put them at high risk of acquiring HIV infection; the proposed study population should reflect the socioeconomic, racial, and ethnic female populations infected with HIV.

#### MECHANISM OF SUPPORT

Applications funded under this RFA will be supported through the National Institutes of Health (NIH) cooperative agreement (U01). Cooperative agreements are awarded to institutions when it is desired to encourage investigator-initiated research in areas of special importance to the NIH and where substantial programmatic involvement by NIH staff is anticipated. The interaction of NIAID staff with the investigators is expected to assist and facilitate the research. This RFA represents a single competition with a specified deadline for receipt of applications. Reissuance of this RFA will be dependent on the state of science and findings at the completion of this cooperative agreement, as well as the availability of funds.

#### FUNDS AVAILABLE

Approximately \$5,000,000 will be available for funding the total costs of the WIHS during its initial year. The earliest possible award date is July, 1993. The NIAID anticipates making two to five awards as a result of this RFA. The final number of awards to be made is dependent upon receipt of a sufficient number of applications of high scientific merit and the continuing availability of funds.

#### BACKGROUND

The number of cases of Acquired Immunodeficiency Syndrome (AIDS) diagnosed in women has increased rapidly since 1985. As of June 1992, more than 24,000 cases of AIDS in women had been reported to the Centers for Disease Control (CDC); in sharp contrast to the approximately 1,100 women reported by the end of 1985. Approximately 100,000 American women are estimated to be infected with HIV-1. These numbers are expected to continue to increase throughout the 1990s. Major deficiencies remain in understanding the clinical, immunological, and virological spectrum of HIV disease and AIDS in women. Gynecological manifestations of HIV infection have not been sufficiently studied despite early results indicating their importance. On the basis of these early reports, women-specific disease outcomes have been identified, suggesting the need for a large-scale prospective study of HIV infection and disease in women to address the multiplicity of research questions within a single research design.

The primary purpose of this RFA is to develop a cooperative multi-site prospective epidemiologic study of the clinical, immunologic, and virologic and behaviorally-associated aspects of HIV disease progression in women. The CDC and NIAID have initiated the initial phase of this interagency prospective study of HIV-infected and uninfected women through the CDC's 1991 program announcement No. 115 (see Federal Register, vol. 56, no. 65, Thursday, April 4, 1991), the HIV Epidemiology Research Study (HERS). The data collection instruments (medical history intake questionnaires, physical exam protocols, and laboratory specimen collection forms) for this phase of the study are being developed collaboratively between the CDC, NIAID, the four currently funded clinical sites, and an interim data center. The data collection instruments developed for the HERS are available on request by faxing your request to Dr. Sandra Melnick at (301) 402-1506. When new sites are awarded under this RFA awardees will collaborate with the investigators from the CDC HERS sites to review the study data collection instruments and physical examination protocols, to arrive at compatible data collection procedures.

#### RESEARCH OBJECTIVES

The overall objectives of this project are to:

- o Describe the spectrum and course of the clinical manifestations of HIV infection in women, including those which may occur in the genital tract and oral cavity.
- o Describe the pattern and rate of decline of CD4+ cells in women and its relationship to other immunologic and virologic parameters, and to the clinical manifestations of HIV.
- o Investigate factors (e.g., infectious, treatment-related, nutritional, socioeconomic, drug-use related) which may delay or may accelerate HIV-induced immune dysfunction and specific manifestations of HIV-associated



clinical disease.

- o Study the length of survival and quality of life of women living with HIV infection.

Although the emphasis of this study is not on transmission of HIV, it will still be important to follow the initially HIV-seronegative women to:

- o Determine the rate of incident HIV seroconversion and factors that may increase the risk of incident HIV infection among a smaller cohort of women who are HIV-antibody negative at the time of study enrollment. Such factors may include age, race, and ethnicity.
- o Assess the feasibility of HIV vaccine trial initiation in HIV-seronegative women by assessing willingness to participate in vaccine efficacy trials.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

NOTE: This study fully meets the requirements for inclusion of women, in that it is exclusively comprised of female subjects.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 11, 1993, a letter of intent that includes a descriptive title of the proposed research the name, address and telephone number of the Principal Investigator; the identities of other key personnel and participating institutions; and the number and title of the RFA in response to which the application may be submitted. The letter of intent is requested to provide an indication of the number and scope of applications to be reviewed. The letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application.



The letter of intent is to sent to

Dr. Sandra Melnick  
Vaccine Trials and Epidemiology Branch  
Division of AIDS  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 2A28  
6003 Executive Boulevard  
Bethesda, MD 20892

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to used in applying for these cooperative agreements.

These forms are available from the institutional offices of sponsored research and Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone 301/496-7441.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, "WOMEN'S INTERAGENCY HIV STUDY", RFA AI-92-12 should be typed on line 2a of the face page of the application form and the "YES" box should be marked.

Submit a signed, typewritten original of the application, including the checklist, and three signed, identical single-sided photocopies, in one package, to

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies must be sent directly to

Dr. Dianne Tingley  
AIDS RRS/SRB/DEA  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 4C16  
Bethesda, MD 20892

Applications must be received by both the Division of Research Grants (DRG) and Dr. Tingley by February 18, 1993. Applications received after February 18, 1993 will be returned to the applicant without review.

#### REVIEW CONSIDERATIONS

This application must be directed toward the objectives identified in the RFA. The primary factors that will be considered in the review of the application will be the demonstrated ability or potential to achieve the recruitment and retention goals, scientific merit of the research plans, and the capability to participate in this multicenter study. The RFA contains important additional information about review procedures and criteria.

#### AWARD CRITERIA

Scientific merit and technical proficiency, based on priority scores assigned by the scientific review group, will be the predominant criteria for determining funding priorities. However, after applications have been approved by the National Advisory Allergy and Infectious Diseases Council, NIAID staff reserves the right to consider the demographic features of the nationwide HIV epidemic among women and study cost-efficiency.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcomed. Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Sandra Melnick  
Vaccine Trials and Epidemiology Branch  
Division of AIDS  
National Institute of Allergy and Infectious Diseases  
Solar Building Room 2A28  
6003 Executive Boulevard  
Bethesda, MD 20892  
FAX: (301) 402-1506

Direct inquiries regarding fiscal matters to:

Ms. Jane Unsworth  
Chief, AIDS Grants Management Section/DEA  
National Institute of Allergy and Infectious Diseases  
Solar Building Room 4B25  
6003 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-7075  
FAX: (301) 480-3780

Direct inquiries concerning the review process and requirements to:

Dr. Dianne Tingley  
AIDS RRS/SRB  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building Room 4C16  
Bethesda, MD 20892  
Telephone: (301) 496-0818  
FAX: (301) 402-2638

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.856, Microbiology and Infectious Disease Research and No. 93.855, Immunology, Allergic and Immunologic Diseases Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52, 45 CFR Part 74, and 45 CFR Part 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### THERAPEUTIC STUDIES OF PRIMARY CENTRAL NERVOUS SYSTEM MALIGNANCIES IN ADULTS

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFA AVAILABLE: CA-93-03

P.T. 34; K.W. 0715035, 0705055, 0740015, 0740020

National Cancer Institute

Letter of Intent Receipt Date: January 15, 1993

Application Receipt Date: March 10, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Cancer Therapy Evaluation Program (CTEP) and the Radiation Research Program (RRP) of the Division of Cancer Treatment (DCT) at the National Cancer Institute (NCI) invite applications for cooperative agreements (U01) from consortia of institutions to perform Phase I and II clinical evaluations of promising new chemotherapeutic or biologic agents for the treatment of primary central nervous system (CNS) malignancies and to perform ancillary laboratory studies of aspects of CNS tumor biology with potential clinical implications. Integrated packages of individual applications are encouraged, with the lead institution of a proposed consortium indicating which participating institutions will provide organizational support, scientific leadership, laboratory capabilities, and/or patient resources. Each consortium of institutions will be referred to as a CNS Consortium (CNCS) for the purpose of this RFA.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Therapeutic Studies of Primary Central Nervous System Malignancies in Adults, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by North American non-profit and for-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, DCT clinical cooperative groups, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

It is essential that applications be submitted as an integrated package from a team or consortium (CNCS) of medical institutions (a minimum of three) that agree to work together with a single Project Leader and a single administration, and submit applications that will be reviewed in relation to the consortium. Together, the institutions in the consortium would encompass experience in investigational drug clinical trials, access to sufficient numbers of primary CNS tumor patients to enter a minimum of 60-80 fully evaluable cases per year onto Phase I and II protocols, expertise in laboratory investigation of the biology of human gliomas, and access to a Central Operations Office for coordination of research activities and data analysis. Except under unusual circumstances, the Central Operations Office/Coordinating Center would be expected to reside at the Project Leader's institution.

#### MECHANISM OF SUPPORT

Awards will be made as cooperative agreements that create an assistance relationship with substantial NCI programmatic involvement with the recipients during the performance of the project, as outlined in this RFA. The cooperative agreement mechanism is used when the NCI wishes to stimulate investigator interest and proposes to advise or assist in an important and opportune area of research.

Support of this program will be through the Cooperative Agreement (U01), an assistance mechanism in which substantial NCI programmatic involvement with the recipient during performance of the planned activity is anticipated. The nature of NCI staff involvement is described in the RFA. Applicants will be responsible for the planning, direction, and execution of the proposed project. Except as otherwise stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

This RFA is a one-time solicitation. However, if it is determined that there is a sufficient continuing program need, the NCI will invite recipients of awards under this RFA to submit competitive continuation cooperative agreement applications for review according to the procedures described in Review Considerations, Part A.

#### FUNDS AVAILABLE

Approximately \$1,500,000 in total costs per year for four years will be committed to specifically fund applications submitted in response to this RFA. It is anticipated that six to nine individual awards will be made to one to three consortia. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications submitted in response to the present RFA may not exceed four years. Although this program is provided for in the financial plans of the NCI, the award of cooperative agreements pursuant to this RFA is also contingent upon the continuing availability of funds for this purpose.

#### RESEARCH OBJECTIVES

The primary goal of this initiative is to stimulate clinical research in the treatment of primary CNS malignancies in adult patients by providing support for consortia of institutions to perform Phase I and II clinical evaluations of promising new chemotherapeutic or biologic agents. A secondary goal is to utilize the consortia as a mechanism for sharing human brain tumor specimens among investigators conducting laboratory studies relevant to the biology, clinical behavior, or therapy of CNS tumors, particularly malignant gliomas.

Clinical trials will take advantage of new developments in drug and radiation resistance, radiation sensitization, biological response modification, immune modulation, induction of apoptosis, differentiation induction, therapeutic irradiation techniques, induction or suppression of specific gene function, or other innovative approaches. Each CNSC will be formed for the purpose of: (1) sharing expertise of researchers in multiple disciplines; (2) conducting joint phase I and II clinical trials to provide adequate patient populations and timely completion; and (3) sharing of tumor specimens and data useful in the conduct of clinical pharmacologic and correlative laboratory studies. Participating institutions in the proposed consortium may be involved in clinical trials and/or laboratory studies.

It is anticipated that one to three consortia will be established, comprising three to nine institutions. Each CNSC will select the specific agents to be tested in accord with their scientific interest and expertise and will develop a series of appropriate Phase II or Phase I trials with supporting protocol documents. Each applicant CNSC should submit as examples one or more draft clinical protocols as supplements to the Central Operations Office/Coordinating Center (Project Leader) and the participant institution applications. The CNSC, along with the assistance of the NCI Program Director, will develop a plan for prioritization of investigational trials. The NCI may provide NCI-sponsored IND agents or provide assistance to the awardee(s) by sponsoring or cross-referencing INDs for selected agents. Each CNSC must have documented numbers of patients with CNS tumors and a history of accrual of patients to clinical trials adequate for two-six phase I or II trials (60-180 patients) per year. It is expected that all of the CNSC institutions together will be able to complete approximately six phase I or phase II trials (180 patients) per year. In addition, proposed consortia must have: (1) adequate radiotherapy support for clinical trials utilizing radiation in combination with other modalities; (2) adequate central data collection and processing capabilities as well as biostatistical expertise; (3) adequate pathology support for both institutional tumor classification and central neuropathology review and for banking and distribution of tumor tissues for concurrent and future laboratory studies; (4) mechanisms to collect and store patient specimens for laboratory studies being conducted by institutions in the CNSC; (5) expertise in antineoplastic drug pharmacology/pharmacokinetics.

The correlative laboratory research program in a CNSC should address at least one field of research into the biology of human malignant gliomas with some potential for future clinical relevance. Examples of research fields for laboratory studies include: molecular genetics and cytogenetics, gene function and expression, signal transduction pathways, radiobiology, growth regulation, metabolism, differentiation and gene modulation by investigational agents, intracellular metabolism, mechanisms of drug resistance in tumor cells, CNS pharmacokinetics, invasion and spread, cytokine production or interactions, immune function and antigen expression, or other aspects that may have clinical implications or lead to new therapeutic approaches. Investigators are not limited to the above areas of laboratory experimentation.

Correlative laboratory studies need not be directly related to individual clinical Phase I/II trials but should attempt to utilize the large clinical database that will be generated by the consortium to identify potential correlates of tumor behavior, and laboratory studies should be based on strong and testable hypotheses. A clear rationale should be given for the experimental design and technological methodologies selected. Preliminary data from appropriate tumor models or analysis of patient specimens should be provided to support the feasibility of each study. The laboratory assays must utilize tumor specimens from patients and there should be an established plan for prioritization of specimen distribution to collaborating laboratories. Participating institutions primarily involved in laboratory studies may accrue patients on CNSC clinical trials if the minimum clinical resources are in place (See ELIGIBILITY REQUIREMENTS).

The cooperative approach outlined in this RFA allows for interactions among successful applicants, with the assistance of NCI extramural staff, to perform Phase I and Phase II trials of anticancer agents and ancillary laboratory studies. This mechanism retains the decision-making prerogatives of the Principal Investigator and his/her colleagues, but at the same time, permits the active participation of NCI in research activities. (See TERMS OF COOPERATION)



For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Project Leader, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. Richard Kaplan at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for cooperative agreements. These forms are available at most institutional offices of sponsored research; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441; and from the NCI Program Director named below.

The Central Operations Office/Coordinating Center as lead institution should submit a research grant application in which they should list the anticipated participant institutions, and include proposed clinical protocols in the Appendix. (The Central Operations Office/Coordinating Center application must be a separate document from any application from a participant institution; if a single institution will be applying for both participation in clinical and/or laboratory studies and as the Central Operations Office/Coordinating Center, two applications will be necessary.) Each participant institution should submit an individual research grant application and should indicate the Central Operations Office/Coordinating Center of the CNSC consortium in which they intend to participate. Participant institutions conducting clinical trials should include copies of the proposed CNSC clinical protocols in the Appendix. The grant application should describe the nature of their participation and justify budget requests for the protocols.

Applications must be received by March 10, 1993. If an application is received after that date, it will be returned. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

#### REVIEW CONSIDERATIONS

##### Review Procedures

Upon receipt, applications will be reviewed for completeness by DRG and responsiveness by the NCI. Incomplete applications will be returned to the applicant without further consideration. Applications that are judged non-responsive will be returned by the NCI. An application judged to be non-responsive to this RFA may be submitted as an investigator initiated regular research grant (R01) or program project grant (P01) at the next receipt date. The application would require modification in accordance with either the R01 or P01 guidelines. The new application would not be considered an application for a Cooperative Agreement, nor would it be considered a response to an RFA. Questions concerning the relevance of proposed research to the RFA may be directed to program staff as described in the INQUIRIES section below.

Applications may be triaged by an NCI peer review group on the basis of relative competitiveness. The NCI will withdraw from further competition those applications judged to be noncompetitive for award and notify the applicant and institutional business official. Those applications judged to be both competitive and responsive will be further evaluated, using the review criteria stated below, for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review will be provided by the National Cancer Advisory Board.

#### AWARD CRITERIA

The anticipated date of award is September 1993. In addition to the technical merit of the application, NCI will consider how well the CNSC and participant institutions met the goals and objectives of the program as described in the RFA.



## INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA and inquiries about whether or not specific proposed research would be responsive are strongly encouraged and may be directed to program staff listed below. The program staff welcome the opportunity to clarify any issues or questions from potential applicants.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Richard Kaplan, Senior Investigator  
Cancer Therapy Evaluation Program  
National Cancer Institute  
Executive Plaza North, Room 734  
Bethesda, MD 20892  
Telephone: (301) 496-8866  
FAX: (301) 480-4663

Direct inquiries regarding fiscal matters to:

Ms. Katharine Schulze  
National Cancer Institute  
Executive Plaza South, Room 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800, ext. 16  
FAX: (301) 496-8601

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No 93.395, Cancer Treatment Research. Awards are made under the authorization of the Public Health Service Act, Title IV Sections 301, 410, and 411, Part A (Public Law 78-410, 42 USC 241 as amended, Public Law 99-158, 42 USC 285a) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## EXPLORATORY GRANTS FOR CENTERS OF EXCELLENCE IN MOLECULAR HEMATOLOGY

NIH GUIDE, Volume 21, Number 41, November 13, 1992

RFA AVAILABLE: DK-93-06

P.T. 34; K.W. 0785070, 1002058, 0780015, 1002045, 0760020, 1016003

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: January 31, 1993  
Application Receipt Date: March 15, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

## PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites applications for Exploratory Grants for Centers of Excellence in Molecular Hematology, to be awarded competitively in Fiscal Year 1993.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Exploratory Grants for Centers of Excellence in Molecular Hematology, is related to the priority areas of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted from domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, or medical centers. Minority individuals and women are encouraged to submit as Principal Investigators. Applications from foreign institutions are ineligible to apply.

## MECHANISM OF SUPPORT

Support of this program will be through the NIH grant-in-aid Exploratory Grant (P20) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this announcement, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement. The anticipated awards will be for one year duration. Requests for support must be limited to no more than \$20,000 in direct costs. Any application exceeding this amount will be returned to the applicant.

The NIDDK anticipates awarding five Exploratory Grants in Fiscal Year 1993 on a competitive basis, contingent upon the availability of appropriated funds. It is anticipated that approximately \$150,000 in FY 93 funds will be available for funding these awards.

#### RESEARCH OBJECTIVES

The objective of Exploratory Grants (P20) is to provide partial funding for the cost of planning and developing meritorious future Centers of Excellence in Molecular Hematology. Centers of Excellence in Molecular Hematology will allow development of the broad range of technologies involved in investigation of genetic diseases and genetic therapy to be brought together in a unified effort. These technologies will draw on knowledge of viruses, cell culture, bone marrow cells, growth factors, animal models, and the molecular basis of genetic diseases.

During the past two decades, major advances have been made in understanding the molecular basis for inherited diseases. Application of sensitive biochemical and molecular techniques has made molecular diagnosis of a significant number of genetic disorders a reality. Now, with these important diagnostic achievements in hand, even greater efforts must be directed toward development of technologies to formulate specific therapies for these debilitating disorders.

The development of Centers as an organizational mechanism will promote the joint efforts both of basic scientists and clinical researchers toward the study of gene structure and function, the structural biology of proteins and the complex biochemistry of protein interaction, the cell and molecular regulation of blood cell formation, and clinical research to test the efficacy and safety of therapeutic strategies derived from basic investigation. These studies will have as their ultimate goal the development of somatic gene therapy or other means of treatment of genetic diseases.

#### STUDY POPULATIONS

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them, and the study design must seek to identify any pertinent gender or minority population differences.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Potential applicants are strongly encouraged to submit a letter of intent no later than January 31, 1993. The letter of intent is to include: (1) name of the Principal Investigator/program director and principal collaborators, (2) descriptive title of the potential application, (3) identification of the organization(s) involved, and (4) reference to RFA DK-93-06.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning the review of applications. It allows NIDDK staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Disease  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083

#### APPLICATION PROCEDURES

Applications are to submitted using form PHS 398 (rev. 9/91), available in the business or grants offices of most academic or research institutions and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441. The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page. Detailed instructions on submission procedures are described of the RFA.

#### REVIEW CONSIDERATIONS

Applications that are complete and responsive to the RFA will be evaluated by an appropriate peer review group convened by the NIDDK in accordance with the usual NIH peer review procedures. Following review, the applications will be given a secondary review by the NIDDK Advisory Council unless not recommended for further consideration by the initial review group. Applications that are incomplete or unresponsive to the RFA will be returned to the applicant.

#### AWARD CRITERIA

The anticipated date of award is September 30, 1993. The criteria to be used in the review of applications and the award of grants are discussed in the RFA.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. Direct inquiries about programmatic issues and request for copies of the RFA to:

David G. Badman, Ph.D.  
Hematology Program Director  
Division of Kidney, Urologic and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A-05  
Bethesda, MD 20892  
Telephone: (301) 496-7458

Direct inquiries regarding fiscal matters to:

Ms. Nancy Dixon  
Grants Management Officer  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 637  
Bethesda, MD 20892  
Telephone: (301) 496-7467

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.849 for DKUHD. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ONGOING PROGRAM ANNOUNCEMENTS

### MINORITY HIGH SCHOOL STUDENT RESEARCH APPRENTICE PROGRAM

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PA NUMBER: PA-92-111

P.T. 34, FF; K.W. 0710030, 0720005

National Center for Research Resources

Application Receipt Date: December 1, 1992

### PURPOSE

The National Center for Research Resources (NCRR), National Institutes of Health (NIH), currently plans to continue and expand the Minority High School Student Research Apprentice Program (MHSSRAP) in 1993. The purpose of the program is to provide minority high school students with a meaningful experience in various aspects of health-related research in order to stimulate their interest in careers in science.

In FY 1993, the program is expanding the science teacher initiative to include not only in-service elementary, middle, junior, and senior high school teachers, but also potential K-12 science teachers in pre-service education programs. Eligible teachers will still be those who are members of a minority group or who teach a significant number of minority students. Teachers may participate in the program for a second year. The hands-on summer research project must be structured to update the teachers' knowledge and skills in modern research tools and techniques as well as to strengthen their teaching skills. The experience should provide teachers the opportunity to bring back to the classroom a sense of the excitement of research that would stimulate students to pursue scientific careers. A longer range goal is to establish year round linkages between pre-service and in-service science teachers, elementary and secondary school students, and biomedical researchers.

Please note, however, that expansion of the program in FY 1993 is contingent on the availability of appropriated funds. Thus, allocations may be reduced below the amount requested in the application. Upon recommendation of the National Advisory Research Resources Council, the NCRR will give preference in making awards to those institutions that can support a summer program having a "critical mass" of at least five or six students.

### ELIGIBILITY REQUIREMENTS

Eligible institutions are those that were eligible for a Biomedical Research Support Grant award in FY 1992 or are awardees of the Minority Biomedical Research Support (MBRS) Program. ALL ELIGIBLE INSTITUTIONS, INCLUDING THOSE NOT CURRENTLY OR PREVIOUSLY FUNDED UNDER THE MHSSRAP, ARE STRONGLY ENCOURAGED TO APPLY. Only one application for the Apprentice Program may be submitted by a component of an institution that is BRSG-eligible in FY 1992 and the recipient of an MBRS award.

Under-represented minority students and teachers are defined as individuals who identify themselves as Black, Hispanic, Native American, Pacific Islander, or any particular ethnic or racial group which has been determined by the grantee institution to be under-represented in biomedical or behavioral research.

Participants eligible for support must be U.S. citizens or have a permanent visa. Eligible students are those

who are enrolled in high school during the 1992-1993 academic year. (Students who will graduate from high school in 1993 are eligible, as is a student who participated in a previous year provided he/she is still enrolled at the high school level.)

#### MECHANISM OF SUPPORT

The mechanism of support for this program will be the NIH grant-in-aid (S03).

Awards will be for one year beginning March 1, 1993, contingent upon availability of appropriated funds. Support will be provided at a level of \$2,000 for each student apprentice, \$3,000 for each pre-service teacher, and \$5,000 for each in-service science teacher. Applications may request both students and teachers or students only. No indirect costs will be paid. Direct support must be as salary; stipends are not allowed. Funds allocated may also be utilized for supplies, extending the research experience, or if adequate funds exist, for the addition of a student apprentice. However, funds from these grants may only be used for the costs of the apprentice program. The Program Director is responsible for the recruitment and selection of the apprentices and science teachers and assignment of each to an appropriate investigator.

Students. Recruitment and selection of students must emphasize factors including the student's motivation, ability, scholastic aptitude, and accomplishments. In addition, consideration must be given to science teachers' recommendations and, whenever possible, the degree of parental commitment. Assignments must be made to investigators involved in health-related research who are committed to increasing the high school student's understanding of research and the technical skills needed.

Teachers. Recruitment and selection criteria for in-service teachers must include: experience and teaching responsibilities, level of interest in participating in a research program, expected impact on their teaching programs, ability to stimulate minority students to pursue scientific careers, and future plans for continued interaction with the research institution. Potential teachers should be enrolled in pre-service programs and have an expressed interest in teaching life sciences at the K-12 level.

#### APPLICATION PROCEDURES

The application consists of (a) a letter stating the justification for the number of student and teacher positions requested (preference will be given to those institutions with a demonstrated commitment and a documented history of encouraging students to pursue scientific careers) and (b) the original and one signed and completed copy of the face page, page 4 "Detailed Budget for First 12-Month Budget Period Direct Costs Only," and checklist page of the grant application form PHS 398 (rev. 9/91). The required pages of the PHS 398 application form must be completed according to instructions provided in the PHS 398 (rev. 9/91) kit except for the following:

##### Face Page

Item 1 - Leave blank.

Items 2a and 2b - Check the box marked "YES" and type in the number and title of this Program Announcement.

Items 4 and 5 - Not applicable; do not complete.

Item 6, Dates of entire proposed project period - Enter 03-01-93 through 02-28-94.

Item 7 and 8 - Insert the total dollar amount of the request, which is the sum, from application page 4, of the number of student positions requested times \$2,000 per student; the number of pre-service teachers requested times \$3,000; and the number of in-service teachers times \$5,000. No indirect costs will be provided; thus the direct and total costs will be the same.

Item 14, Organizational component to receive credit towards a Biomedical Research Support Grant - Use this space to enter the code on which eligibility for this MHSSRAP application is based (no credit will be given for the S03 application). Also use this space to enter the BRSG and/or MBRS grant number(s) if available.

Page 4, "Detailed Budget for First 12-Month Budget Period Direct Costs Only" - Using ONLY the Other Expenses category, enter on separate lines the number of students requested at \$2,000 per student; the number of pre-service teachers requested at \$3,000 per teacher; and the number of in-service science teachers requested at \$5,000 per teacher.

Enter the sum of the amounts requested for each under the "TOTALS" column for the Other Expenses category and under "Total Direct Costs for First 12-Month Budget Period" at the bottom of the page.

The original and one copy of the student and teacher report(s), signed by the Program Director, must be submitted with the renewal application by December 1 so that the data contained in these reports can be used by NCRR to decide about policies and future funding for the MHSSRAP.

These reports must also be submitted at the same time even if renewal support is not requested. All reports, including the Financial Status Report, must be submitted to the NIH by the grantee institution no later than May 31, 1993, unless an extension of the budget period end date has been authorized in writing.

Applications must be received by December 1, 1992 by:

Office of Grants and Contracts Management  
National Center for Research Resources  
Westwood Building, Room 849  
5333 Westbard Avenue  
Bethesda, MD 20892



(Do NOT mail the application to the Division of Research Grants, NIH.)

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Marjorie A. Tingle, Ph.D.  
Director, Biomedical Research Support Program  
National Center for Research Resources  
Westwood Building, Room 10A-11  
5333 Westbard Avenue  
Bethesda, MD 20982  
Telephone: (301) 496-6743.

Direct inquiries regarding fiscal matters to:

Ms. Mary V. Niemiec  
Office of Grants and Contracts Management  
National Center for Research Resources  
Westwood Building, Room 849  
5333 Westbard Avenue  
Bethesda, MD 20982  
Telephone: (301) 496-9840

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.337, Biomedical Research Support. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (a)(3); Public Law 78-410 (42 USC 241) as amended, and administered under PHS grants policies and Federal Regulations 45 CFR 74 and the Guidelines for Minority High School Student Research Apprentice Program. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***



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# NIH GUIDE

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Vol. 21., No. 41, Part II of II  
November 13, 1992

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National Institute of Health





ONGOING PROGRAM ANNOUNCEMENTS

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

ONGOING PROGRAM ANNOUNCEMENTS

MOLECULAR AND CELLULAR BIOLOGY OF METASTATIC TUMOR CELLS

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PA: PA-93-016

P.T. 34; K.W. 0715035, 1002004, 1002008

National Cancer Institute

PURPOSE

The National Cancer Institute (NCI) invites exploratory/developmental grant applications to study the molecular and cellular biology of metastatic tumor cells. This special initiative is designed to promote collaborations and facilitate scientific interchange between investigators, one with experience in the biology of metastasis and the other in a more basic scientific discipline such as molecular or cellular biology, or biochemistry. Therefore, prospective Principal Investigators need to identify a research collaborator.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Molecular and Cellular Biology of Metastatic Tumor Cells, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

MECHANISM OF SUPPORT

Support of this program will be through the National Institutes of Health (NIH) exploratory/development research grant (R21). Applicants will be responsible for the planning, direction, and execution of the proposed project. Awards will be administered under PHS policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990 and in this PA.

The Exploratory/Developmental Research Grants program (R21) provides limited funds for short-term research projects. These grants provide an opportunity for initiating studies that may be preliminary in nature. Research investigators in relevant fields are invited to apply for these grants in order to develop preliminary data that could form the basis of future research project grant (R01) applications.

The Principal Investigator must be accountable to the recipient organization officials for the proper conduct of the project. The research collaborator must be named and time and effort listed on the budget page. The recipient organization is legally responsible and accountable to the PHS for performance and financial aspects of the grant-supported activity.

#### FUNDS AVAILABLE

The direct costs per year for each application funded by the NCI must not exceed \$50,000. The total project period for applications submitted in response to this PA may not exceed two years and is not renewable. Applicants are advised to contact other relevant funding components regarding their funding policies.

#### RESEARCH OBJECTIVES

The goal of this initiative is to provide funds for preliminary research projects that will form the basis of future R01 applications to investigate metastasis. The intent is to (1) foster collaborative research between investigators with basic molecular and cellular biological and biochemical research experience, and those with experience in metastasis research, and (2) increase the number of laboratories and investigators addressing issues of metastasis.

The scope of the research may encompass the application of any aspect of molecular and cellular biology and biochemistry to the investigation of metastasis biology. Applications should be for preliminary data gathering or pilot feasibility studies, and should be founded on the combined research experience of the Principal Investigator and his/her collaborator. The application should specifically address how the application meets the intent of the initiative, e.g., the development of a new collaboration between an investigator with basic molecular and cellular biological and biochemical research experience and one with experience in metastasis research. Furthermore, the research collaborator should address how the proposed research will relate to and integrate with other ongoing research in his/her laboratory. Just as the initiative is intended to foster a research collaboration, the application itself should clearly be the product of in-depth discussions and input from both the research collaborator and the Principal Investigator.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. Applications will be accepted at the three regular application deadlines as indicated in the application kit. These forms are available at most institutional offices of sponsored research; from the Office of Grant Inquiries, Division of Research Grants (DRG), National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone 301/496-7441; from the NCI Program Director named below. The title and number of the PA must be typed in section 2a on the face page of the application.

The completed original application and five exact copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892

#### REVIEW PROCEDURE

Upon receipt, applications will be reviewed by the DRG for completeness. Incomplete applications will be returned to the applicant without further consideration. Those applications judged to be complete will be further evaluated for scientific and technical merit by study sections of the DRG. Following the scientific and technical review, the applications will receive a second level of review by the appropriate national advisory council.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following factors will be considered when making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the PA.

The following additional factors will be considered for applications assigned to the NCI:

- o In order to increase the number of laboratories and investigators with potential for a long-term commitment to metastasis research, preference in funding will be given to those investigators that are early in their research careers
- o The extent to which the proposed research develops collaborations that address the purpose of the initiative
- o How the proposed research relates to and integrates with other ongoing research in the research collaborator's laboratory

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Suresh Mohla  
Chief, Cancer Biology Branch  
National Cancer Institute  
Executive Plaza South, Room 630  
Bethesda, MD 20892  
Telephone: (301) 496-7028  
FAX: (301) 402-1037

Direct inquiries regarding fiscal and administrative issues to:

Robert Hawkins  
Grants Management Branch  
National Cancer Institute  
Executive Plaza South, Room 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800 ext. 13

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No.93.396, Cancer Biology. Awards are under authorization of the Public Health Service Act, Title, IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grant policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive order 12372 or Health Systems Agency review.

## OXIDATIVE DAMAGE, ANTIOXIDANT DEFENSE, AND AGING

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PA: PA-93-017

P.T. 34; K.W. 0710010, 0765035, 0760070, 0765025

National Institute on Aging

## PURPOSE

Free radical damage has long been believed to be a risk factor for the degenerative processes that accompany aging in a variety of animal species ranging from insects to humans. The free radical theory of aging was proposed by Denham Harman in 1956, and much research since then has been directed towards establishing correlations among oxidative damage, antioxidant defense systems, aging and life span. Although a few modest correlations have been observed, efforts to move beyond correlative evidence, e.g., using antioxidant manipulations in animal and cell culture models to attempt to extend maximum life spans, have yielded few definitive results. Nevertheless, evidence continues to accumulate about the ubiquity of free radicals and their considerable destructive potential in living tissues. It is plausible that an improved understanding of free radical processes will lead to the discovery of interventions (dietary, pharmacological or genetic) to improve health and increase life spans. Research is needed to establish the critical relationships among free radical sources, protective systems and aging phenomena that may be amenable to intervention.

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

Foreign institutions are not eligible to apply for career awards (K04, K08, K11) or First Independent Research Support and Transition (FIRST) (R29) awards, and can apply for National Research Service Training Awards (F32, F33) only if the applicant is a U.S. citizen. Applicants for F32, F33, K04, K08, and K11 awards must be U.S. citizens or resident aliens.

## MECHANISMS OF SUPPORT

The primary mechanisms for support of this program are:

- o Research grant (R01)
- o FIRST award (R29)
- o Career grants, which include: Research Career Development Award (K04); Clinical Investigator Award (K08); Physician Scientist Award, individual (K11)
- o Fellowships (F32, F33)

Deadlines for applications are as follows:

F-series grants:	Jan 10, May 10, and Sep 10
New R and K-series grants:	Feb 1, Jun 1, and Oct 1
Competing continuation and revised grants:	Mar 1, Jul 1, and Nov 1

## RESEARCH OBJECTIVES

The National Institute on Aging (NIA) invites investigators to submit applications for research on oxidative damage and pathobiology as related to aging and the aging process. Priority will be given to research projects that are likely to provide critical insights into these relationships other than correlative data. Also, it is recognized that the National Cancer Institute (NCI) has an interest in the role of oxidative damage in cancer and the carcinogenesis process, the National Institute of Environmental Health Sciences (NIEHS) has an interest in toxic environmental agents, and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has an interest in the role of oxidative damage due to saturated and unsaturated lipids on normal and abnormal metabolic processes in high eukaryotes and humans. Applications will be given an institute assignment based on the Referral Guidelines for Funding Components of PHS.

The following areas of research are of particular interest to the NIA, but applications need not be limited to the areas listed below.

1. Improved methods for measuring any of the following in biological tissues suitable for aging studies: levels of antioxidants in both the oxidized and reduced state; rate of production of superoxide, hydrogen peroxide and hydroxyl radical; levels and/or identification of oxidized products in macromolecules, such as DNA, protein and lipids; rate of repair of oxidized macromolecules in vivo.
2. Identification of which enzyme activities involved in antioxidant defense are rate-limiting, with particular emphasis on age-related changes.
3. The role of heavy metal ions, whether bound or free, in age-related accumulation of oxidative damage in vivo.
4. Development of interventions that reduce oxidative damage through either neutralization of oxygen free radicals, reduction of the rate of production of oxygen free radicals, repair of oxidative damage, or improvement of antioxidant defense systems, coupled with a demonstration that this reduced oxidative stress is associated with a change in age-associated biological processes and/or diseases.
5. The role of mitochondrial dysfunction in cellular oxidative damage due to normal metabolism, and how this changes with age.
6. Elucidation of how genes involved in antioxidant defense systems are regulated in vivo, with particular emphasis on how the regulation is altered during aging.
7. The mechanism of attenuation of oxidative damage by spin trapping compounds and other chemical and dietary interventions.
8. Determination of whether and/or how caloric restriction reduces oxidative damage, and whether or not this is related to life span extension.
9. The relationship between oxidative damage and the eventual development of age-related disease states.
10. Development of animal model systems, particularly transgenic animals, to test the effect of altering oxidative damage or antioxidant defense systems on aging and/or life span.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided. The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 3, Recruitment of Individuals from Under represented Racial/ethnic Groups, and Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups.

However, NIH recognizes that it may not be feasible or appropriate in ALL research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans including American Indians or Alaskan Natives, Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention and preventive strategies, diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.



The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application. All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications for R01, R29, and K Awards are to be submitted on the grant application form PHS 398 (rev.9/91) and will be accepted at the standard application deadlines indicated in the application kit. Applications for F32 and F33 awards are to be submitted on form PHS 416 (rev. 10/91).

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies of PHS 398 or two copies of PHS 416 must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

To expedite the application's routing within the NIH, please check the box on the face page of the application indicating that the application is in response to this announcement and type (next to the checked box) "Oxidative Damage and Aging."

Applications for F32, F33 and R29 awards must include at least three letters of reference attached to the face page of the original application. Applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

#### REVIEW CONSIDERATIONS

The review criteria are the traditional considerations underlying scientific merit. Applications will be assigned on the basis of established Public Health Service referral guidelines. For information on the special review criteria for the FIRST (R29) award, research career awards (K series), and fellowships (F32, F33) contact the program staff listed under INQUIRIES. Applications will be assigned on the basis of established PHS referral guidelines. In accordance with the standard NIH peer review procedures, research project grant (R01 and R29) applications, fellowships (F32, F33) and research career development awards (K04) will be reviewed for scientific and technical merit by an appropriate study section in the Division of Research Grants. Other applications (K08 and K11) will be reviewed by an appropriate institute review group. Following scientific/technical review, the applications will receive a second-level review by the appropriate advisory council.

#### AWARD CRITERIA

There are no set-aside funds for funding these applications. Applications compete for available funds on the basis of scientific merit with all other applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Researchers considering an application in response to this announcement may discuss their project and the range of grant mechanisms available with NIA staff in advance of formal submission. This can be done either through a telephone conversation or a brief letter giving the descriptive title of the proposed project and identifying the Principal Investigator and, when known, other key participants. Applications related to the health of women and minorities are particularly encouraged. Correspondence and inquiries may be directed to:

Huber R. Warner, Ph.D.  
Biology of Aging Program  
National Institute on Aging  
Gateway Building, Room 2C231  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-6402  
FAX: (301) 402-0010

or

Pamela Starke-Reed, Ph.D.  
Geriatrics Program  
National Institute on Aging  
Gateway Building, Room 3E327  
7201 Wisconsin Avenue  
Bethesda, MD 20892  
Telephone: (301) 496-6761  
FAX: (301) 402-1784

Direct inquiries regarding fiscal matters to:

Joseph Ellis  
Grants and Contracts Management Officer  
National Institute on Aging  
Gateway Building, Room 2N212  
Bethesda, MD 20892  
Telephone: (301) 496-1472

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive order 12372 or Health Systems Agency review.

#### NEURAL REGENERATION AND PLASTICITY AFTER SPINAL CORD INJURY

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PA: PA-93-018

P.T. 34; K.W. 0715027, 0705055, 1002030, 0760015

National Institute of Neurological Disorders and Stroke

#### PURPOSE

The Division of Stroke and Trauma (DST), National Institute of Neurological Disorders and Stroke (NINDS), invites applications for support of research that will increase our knowledge of the mechanisms underlying the neuronal regeneration and plasticity that can follow spinal cord injury.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Neural Regeneration and Plasticity after Spinal Cord Trauma, is related to the priority area of unintentional injuries: spinal cord injury. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic institutions, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority institutions, minority individuals, and women are particularly encouraged.

#### MECHANISMS OF SUPPORT

The support mechanism for grants in this area will be the traditional investigator-initiated research project grant (R01). The Principal Investigator will plan, direct, and, along with any co-investigators, perform the research. Applicants are encouraged to contact the NINDS representative listed below as early as possible in the planning stages.

## RESEARCH OBJECTIVES

### Background

Injury to the spinal cord tragically affects hundreds of thousands of victims in the United States, with approximately 10,000 new traumatic injuries each year. Early treatment and improved hospital care have increased survival, but at great cost. The estimated yearly cost of long term, specialized care for paralyzed patients exceeds \$2 billion. The personal costs to patients and their families is beyond calculation: planned education, career, marriage, and independence are interrupted and often never regained.

The spinal cord, as part of the central nervous system (CNS), coordinates movement and sensation for the entire body below the head. Specialized cell populations within the cord are the substrates for these functions. Large motoneurons extend long axons peripherally to innervate skeletal muscle. Extensive arborizations of these motoneurons receive information via descending tracts from the brain. The long fibers of dorsal root ganglion cells connect peripheral sensory receptors to spinal interneurons, to motoneurons, and to brain centers. This complex neuronal circuitry of the spinal cord is supported by the glia of the CNS. Radial glia enclose the cord like the rim and spokes of a wheel, defining compartments for ascending and descending fiber systems. Astrocytes contribute to the blood-spinal cord barrier and provide a wide variety of support functions. Oligodendrocytes myelinate axons.

Traumatic injury disrupts all of these cell types and changes their functions. Axons degenerate, neurons die, astrocytes proliferate and become reactive, radial glia enclose large cysts, and oligodendrocytes cannot remyelinate damaged areas. The anatomy of an injured spinal cord shows profound pathology, but also reveals the sprouting of uninjured fibers, the regeneration of damaged populations, the reorganization of glia, and clearing away of debris.

Enhancement of these beginnings of regeneration and reorganization is necessary. Several trophic factors are known to affect survival of neurons and extension of neurites. Likewise, naturally occurring substances may enhance supportive glial functions. Components of the extracellular matrix can support the growth of axons. The growing knowledge of cellular mechanisms of repair within the injured spinal cord offers the hope of treatment for this devastating disorder.

### Research Goals and Scope

Examples of investigator-initiated research grant applications for basic, applied, and clinical studies related to the understanding and enhancement of regeneration in the injured spinal cord may include, but should not necessarily be limited to:

- o identification of the tissues, cells, and substrates critical to the regenerative process;
- o behavioral, chemical, functional, and structural correlates of restored or remodeled neural circuits;
- o gene and protein expression in neurons and support cells during regeneration;
- o development of cellular transplants to augment or support regeneration, restore lost function, or replace damaged cells;
- o immune responses to implants of neural tissues, cell lines, or cellular products; and
- o pharmacological or biochemical approaches to prolong or enhance regeneration.

Applicants are encouraged to develop and use new or refined methodologies, instrumentation, and procedures that will reveal mechanistic details of the regenerative process. Basic, applied, or clinical studies on interventions or manipulations to improve regrowth of fibers, prevent pathophysiological changes, or aid in functional recovery are welcome.

### POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders, and conditions that disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial or ethnic group. In addition, gender and racial or ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups; however, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial or ethnic minority populations: Native Americans (including American Indians or Alaska Natives), Asian or Pacific Islanders, Blacks, and Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and prevention strategies), diagnosis, or treatment of diseases, disorders, or conditions, including, but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded; however, every effort should be made to include human tissues from women and racial or ethnic minorities when it is important to apply the results of the study broadly. This directive should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully. Since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) according to the instructions included in the application package. These application packages are available at the business offices of most institutions eligible to receive Federal grants and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Receipt dates for new research project grant applications (R01) are February 1, June 1, and October 1.

On page 1 of form PHS 398, check "yes" in Item 2a, enter the number of this Program Announcement in the space provided, and provide the name of this Program Announcement, Neural Regeneration and Plasticity after Spinal Cord Injury in the blank space labeled "Title."

Use the mailing label provided in the application package to mail the signed original and five exact copies of it to:

Division of Research Grants.  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Applications will be reviewed for scientific and technical merit by an appropriate study section in the Division of Research Grants. The second level of review will be by the appropriate national advisory council. The standard review criteria will be used to assess the scientific merit of applications.

#### AWARD CRITERIA

Applications will compete for available funds with other applications assigned to an Institute or Center. The following will be considered when making funding decisions:

- o quality of the proposed projects as determined by peer review
- o availability of funds
- o program balance among research areas.

#### INQUIRIES

Questions concerning scientific aspects of this Program Announcement may be addressed to:

Dr. Mary Ellen Michel  
Division of Stroke and Trauma  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 8A13  
Bethesda, MD 20892  
Telephone: (301) 496-4226  
FAX: (301) 480-1080

Questions concerning fiscal aspects of this Program Announcement may be addressed to:

Mr. King P. Bond, Jr.  
Division of Extramural Activities  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
Bethesda, MD 20892  
Telephone: (301) 496-9231  
FAX: (301) 402-0219



## AUTHORITY AND REGULATIONS

This program is described in the Catalogue of Federal Domestic Assistance No. 93.853, Clinical Research Related to Neurological Disorders, and No. 93.854, Biological Basis Research in the Neurosciences. Grants will be awarded under the authority of the Public Health Service Act, Title IV, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR 74. This program is not subject to Health Services Agency Review of the intergovernmental review requirements of Executive Order 12372.

## NEUROLOGICAL BASIS OF RECURRENT HEADACHE, ESPECIALLY MIGRAINE

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PA: PA-93-019

P.T. 34; K.W. 0715138, 0765035, 0760025, 0755030, 0745027, 0411005

National Institute of Neurological Disorders and Stroke

### PURPOSE

The Division of Stroke and Trauma (DST), National Institute of Neurological Disorders and Stroke (NINDS), invites applications for support of research that will increase our understanding of the causes of, and add to our ability to treat and prevent, recurrent headache, especially migraine.

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic institutions, for-profit and non-profit organizations, public or private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the Federal government. Foreign institutions are eligible to apply for research project grants (R01) only. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards. Applications from minority institutions, minority individuals, and women are particularly encouraged.

### MECHANISMS OF SUPPORT

The support mechanisms for grants in this area will be the traditional investigator-initiated research project grant (R01), the FIRST award (R29), the program project grant (P01), and the center grant (P50). As consistent with the aforementioned mechanisms, the Principal Investigator or program director, as well as any participating investigators, will plan, direct, and perform the research. Applicants for program project grants should contact the NINDS representative listed below as early as possible in the planning stages.

### RESEARCH OBJECTIVES

#### Background

Millions of Americans suffer from recurrent headaches. For many, the headaches are of such severity that they are disabling. In addition to the profound effects on the quality of life for these people, the economic consequences are enormous. Some estimates are that headache sufferers seek medical care through over eight million visits to physicians or emergency rooms each year. Other estimates of the impact of this condition are that migraineurs alone lose over sixty million workdays a year. A major research goal of the NINDS, which is the responsible agency for neurological research in the Federal Government, is to understand the basic pathophysiology of headaches and to use this understanding to improve methods for treatment and prevention of recurrence.

Headaches can be classified as vascular headaches, muscle contraction headaches, tension headaches, or inflammatory headaches, to mention but a few. Vascular headaches are thought to involve abnormal function of the brain's blood vessels or vascular system. The most common type of vascular headache is migraine headache, the cause of which is still not known. Migraine headaches are frequently characterized by severe pain on one or both sides of the head, nausea, and extreme sensitivity to light and noises. The two most prevalent types of migraine headache are the classic migraine and the common migraine. The major difference between these two types of migraine is that the victim of a classic migraine experiences an aura about 10 to 30 minutes before the onset of headache. This aura is the major prodromal neurological symptom and warning of the imminent onset of the classic migraine. The pain of a migraine headache is described as an intense, throbbing, or pounding pain in the forehead, temple, ear, jaw, or around the eye; these pains may continue for several days. The common migraine is not preceded by an aura; however, some people who are subject to the common migraine exhibit a variety of vague symptoms before the onset of the headache, such as mood shifts, fatigue, and abnormal retention of fluids. The pain of common migraine can also last several days, during which the victim may have nausea or vomiting.

#### Research Goals and Scope

Examples of investigator-initiated research grant applications for basic and clinical studies related, in the broadest sense, to the etiology, prevention, and treatment of recurrent headache, especially migraine headache, may include, but should not necessarily be limited to:

- o precise elucidation of the cellular and molecular events that cause or lead to headaches;

- o development of more specific clinical interventions for both prevention and treatment of migraine headaches, such as anti-platelet clumping drugs; more efficacious anti-serotonin drugs or other means of preventing or reducing the constriction of arteries; and site-specific anti-prostaglandins;

- o development of methods for precisely identifying the sequence of alterations in blood flow or vascular reactivity that may be an initiating factor for migraine;

- o identification of risk factors, or events, that predispose the migraineur to an attack, such as stress, allergies, diet, sleeping patterns, neuroses, personality type, and behavioral characteristics such as excitability and compulsiveness;

- o control of risk factors in relation to the prevention of a migraine headache;

- o longitudinal epidemiology of the distribution and inter-relation between risk factors and the predisposition to an attack of migraine headache;

- o determination of whether or not genetic factors predispose to migraines, and, if so, identification of the genetic locus with a view toward understanding the causative or contributory mechanisms and developing a means of preventing migraine headache; and

- o determination of the relation between hormones and migraine.

#### POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders, and conditions that disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial or ethnic group. In addition, gender and racial or ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups; however, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial or ethnic minority populations: Native Americans (including American Indians or Alaska Natives), Asian or Pacific Islanders, Blacks, and Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and prevention strategies), diagnosis, or treatment of diseases, disorders, or conditions, including, but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded; however, every effort should be made to include human tissues from women and racial or ethnic minorities when it is important to apply the results of the study broadly. This directive should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully. Since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' population, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to the NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION AND REVIEW PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) according to the instructions included in the application package. These application packages are available at the offices of sponsored research of most institutions eligible to receive Federal grants and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

Applicants for program project grants should request, from the address below, a copy of the NINDS Guidelines: Program Project and Research Center Grants (rev. June 1992). Receipt dates for new research project grant applications and FIRST Awards (R01 and R29, respectively) and for program project and center grant applications (P01 and P50, respectively) are February 1, June 1, and October 1.

FIRST award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

On page 1 of form PHS 398, check "yes" in Item 2a, enter the number of this Program Announcement in the space provided, and provide the name of this Program Announcement (Neurological Basis of Recurrent Headaches, Especially Migraine) in the blank space labeled "Title."

Use the mailing label provided in the application package to mail the signed original and five exact copies to the Division of Research Grants. If the application is for a program project or center grant, please send the original and three copies to the Division of Research Grants. An additional two copies of the program project or center grant application sent to the address below would be useful for expediting the processing of these applications for multidisciplinary efforts.

#### REVIEW CONSIDERATIONS

Research project grant applications and FIRST award applications (R01 and R29, respectively) will be reviewed for scientific and technical merit by an appropriate study section in the Division of Research Grants. Program project grant and center grant applications (P01 and P50, respectively) will be reviewed according to the practice of the Institute to which the application is assigned. The second level of review will be by the appropriate National Advisory Council. The standard review criteria will be used to assess the scientific merit of applications.

#### AWARD CRITERIA

Applications will compete for available funds with all other applications. The following will be considered when making funding decisions:

- o quality of the proposed projects as determined by peer review
- o availability of funds
- o program balance among research areas

#### INQUIRIES

Questions concerning scientific aspects of this PA may be addressed to:

Dr. George N. Eaves  
Division of Stroke and Trauma  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 8A13  
Bethesda, MD 20892  
Telephone: (301) 496-4226  
FAX: (301) 480-1080

Questions concerning fiscal aspects of this PA may be addressed to:

Ms. Kathleen Howe  
Division of Extramural Activities  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
Bethesda, MD 20892  
Telephone: (301) 496-9231  
FAX: (301) 402-0219

#### AUTHORITY AND REGULATIONS

This program is described in the Catalogue of Federal Domestic Assistance, No. 93.853, Clinical Research Related to Neurological Disorders, and 93.854, Biological Basis Research in the Neurosciences. Grants will be awarded under the authority of the Public Health Service Act, Title IV, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR 74. This program is not subject to Health Services Agency review of the intergovernmental review requirements of Executive Order 12372.

#### SMALL INSTRUMENTATION GRANTS PROGRAM

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PA: PA-93-020

P.T. 34; K.W. 0735000, 1002024, 0735015, 1014001

National Institutes of Health

Application Receipt Date: February 10, 1993

#### PURPOSE

The National Institutes of Health (NIH) has supported a Small Instrumentation Grants Program (SIP) since FY 1987 in response to several studies indicating that the state of biomedical research instrumentation had seriously eroded over the recent past and that this situation is retarding the progress of biomedical research. The most



significant need identified in these studies is for the relatively low-cost pieces of equipment in the price range of approximately \$5,000 to \$60,000.

Approximately \$6 million will be available from the NIH in FY 1993 for the SIP. (As of October 1, 1992, the NIH was expanded to include the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, and the National Institute of Mental Health and these three institutes will participate in this program.)

#### ELIGIBILITY REQUIREMENTS

Eligible organizations or organizational components are those domestic, non-profit organizations that: (1) received at least three NIH (including the three Institutes indicated above) research grants in the research grants base (defined below) totaling between \$200,000 and \$2,924,000 in FY 1992, and (2) have active NIH research grant support. The "research grants base" is defined as those grants awarded with the following activity codes: K01, K02, K04, K05, K06, K08, K11, K12, K14, K15, K16, K20, K21, P01, P40, P41, P42, P50, P60, R01, R03, R10, R21, R22, R23, R24, R29, R35, R37, R55, S06, S14, U01, U10, U24, U41, U42, and U54.

#### MECHANISM OF SUPPORT

The mechanism of support for this program will be the small instrumentation program (S15). Applicants will be responsible for identifying and purchasing the equipment requested for use on active NIH research grants.

#### APPLICATION PROCEDURES

Only those organizations or organizational components receiving a LETTER OF INVITATION TO APPLY are eligible for a SIP award. These letters, which will contain application instructions, will be mailed on or about November 25, 1992.

Only one application may be submitted from each eligible organization or organizational component, which may establish its own procedures for identifying equipment requests.

Investigators interested in participating in their organization's or organizational component's application should contact the official responsible for completing the application. Those officials who expect to be involved in preparing an application should publicize the availability of SIP funds, so that investigators in need of small research instruments are provided the opportunity to indicate their needs for such equipment.

The SIP award will be restricted to the purchase of equipment costing between \$5,000 and \$60,000. Awards will be made on or before September 1, 1993. The amount of the award will be based on a percentage of the organization's or organizational component's research grants base for FY 1992 or \$5,000, whichever is greater. Organizations or organizational components will be notified of the maximum amount for which they may apply.

Completed applications must be received by February 10, 1993.

#### REVIEW CONSIDERATIONS

Applications will be assigned to individual NIH Institutes and Centers for administrative review of the completeness of the application in accordance with the application instructions. Incomplete applications will be returned to the applicant without further consideration. Specific funding decisions will depend on available funds and the appropriateness of the request in relation to active NIH research grant support.

#### INQUIRIES

Issues NOT ADDRESSED in the application instructions may be addressed to:

Research Training and Special Programs Office  
Office of Extramural Research  
National Institutes of Health  
Building 31, Room 5B44  
Bethesda, MD 20892  
Telephone: (301) 496-1968  
FAX: (301) 496-0166

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.337, Biomedical Research Support. Grants will be available under the authority of and administered in accordance with the PHS Grants Policy Statement and Federal regulations at 42 CFR 52 and 42 USC 241. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.



ACADEMIC AWARD IN VASCULAR DISEASE

NIH GUIDE, Volume 21, Number 41, November 13, 1992

PAR NUMBER: PAR-93-008

P.T. 34; K.W. 0715040

National Heart, Lung, and Blood Institute

This change is issued for PAR-93-008, Academic Awards in Vascular Disease which was published in the NIH Guide for Grants and Contracts, Vol. 21, No. 37, October 16, 1992). The fifth sentence under the section ELIGIBILITY REQUIREMENTS should read:

"An individual institution may submit an application for a systemic vascular program OR an application for a pulmonary vascular program for a given receipt date."

The NHLBI will accept only one application per institution, and will make only one award per institution.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

5333 Westbard Avenue  
Bethesda, MD 20816

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# NIH GUIDE

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21, No. 42  
November 20, 1992

RICHARD W. BURR

\* 34010\*  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
CAITHERSBURG MD 20819 0000

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

# NOTICES

## AVAILABILITY OF HUMAN LIVER FOR SCIENTIFIC INVESTIGATION

NIH GUIDE, Volume 21, Number 42, November 20, 1992

P.T. 34; K.W. 0780025, 0765035

National Institute of Diabetes and Digestive and Kidney Diseases

The Liver Tissue Procurement and Distribution System (LTPADS) is a National Institutes of Health (NIH) service contract to obtain human liver from regional centers for distribution to scientific investigators throughout the United States. These regional centers have active liver transplant programs with human subjects approval to provide portions of the resected pathologic liver for which the transplant is performed. Human pathologic liver prepared according to the investigator's specifications provides the opportunity to verify if animal liver investigations are relevant to human liver pathophysiology. The preparation of these livers has been excellent for the usual molecular biologic techniques. Therefore, we are primarily interested in soliciting proposals from investigators interested in studying pathologic liver specimens. Examples would include a particular metabolic disorder or disease entity or the general process of cirrhosis. A limited supply of "normal" liver specimens may also be requested but the turn around time for completion of large requests for "normal" liver is much longer than for pathologic liver specimens.



## INQUIRIES

Further information and proposal forms for interested investigators can be obtained from:

Harvey L. Sharp, M.D.  
Principal Investigator, Liver Tissue Procurement and Distribution System  
c/o Elizabeth Webster  
Box 179 UMHC  
University of Minnesota Hospitals  
Minneapolis, MD 55455  
Telephone: (612) 624-1133

## WORKSHOP ON MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

NIH GUIDE, Volume 21, Number 42, November 20, 1992

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health (NIH), Office for Protection from Research Risks (OPRR), is continuing to sponsor workshops on implementing the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Each of the workshops scheduled for FY 1993 will focus on a specific theme.

The workshops are open to institutional administrators, members of Institutional Animal Care and Use Committees, laboratory animal veterinarians, investigators and other institutional staff who have responsibility for high-quality management of sound institutional animal care and use programs.

Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR representatives.

DATE: DECEMBER 3-4, 1992

TOPIC: MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS

### LOCATION:

Loews Vanderbilt Plaza  
2100 West End Avenue  
Nashville, TN 37203  
Telephone: (615) 320-1700  
FAX: (615) 320-5019

### SPONSORS:

Vanderbilt University  
Meharry Medical College

### REGISTRATION:

Ms. Marilyn Dasaro  
Division of Continuing Medical Education  
Vanderbilt University  
D-8211 Medical Center North  
Nashville, TN 37232-2337  
Telephone: (615) 322-4030  
FAX: (615) 343-0809

## NOTICES OF AVAILABILITY (RFPs AND RFAs)

## RESEARCH AND DEVELOPMENT PROJECTS IN CHEMOPREVENTION

NIH GUIDE, Volume 21, Number 42, November 20, 1992

RFA AVAILABLE: CA-93-05

P.T. 34; K.W. 0745003, 0715035

National Cancer Institute

Letter of Intent Receipt Date: December 9, 1992

Application Receipt Date: February 9, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

### PURPOSE

The Division of Cancer Prevention and Control (DCPC), National Cancer Institute (NCI), invites applications for cooperative agreements to encourage coordinated submissions of related projects from investigators who want to collaborate on studies dedicated to developmental research in chemoprevention.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Research and Development Projects in Chemoprevention, is related to the priority area of chemoprevention. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

Each application will be considered on its own merit as an individual research project. Applicants for Research and Development Projects (RDPs) in Chemoprevention MAY NOT concurrently submit R01 applications that represent significant duplication of the efforts described in the applicant's RDP.

#### MECHANISM OF SUPPORT

This RFA will use the cooperative agreement (U01) mechanism. The cooperative agreement is an assistance mechanism in which substantial NIH programmatic involvement with the recipient during performance of the planned activity is anticipated. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant/awardee. Except as otherwise stated in this RFA, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

This RFA is a one-time solicitation. Future unsolicited competitive continuation applications will compete with all other investigator-initiated research applications and be peer reviewed by a study section in the Division of Research Grants (DRG), NIH. However, if it is determined that there is a sufficient continuing need, the NCI will invite recipients of awards made in FY 93 under this RFA to submit competitive continuing applications for review according to procedures described below in the APPLICATION PROCEDURES and REVIEW CONSIDERATIONS sections.

An assistance relationship will exist between NCI and the awardees to accomplish the purpose of the activity. The recipients will have primary responsibility for the development and performance of the activity. However, there will be government involvement with regard to (1) assistance in securing an Investigational New Drug (IND) approval from the Food and Drug Administration (FDA), (2) coordination and assistance in obtaining the chemopreventive agent, (3) monitoring of safety and toxicity and, (4) quality assurance of the clinical chemistry aspects of the study. Awards will not be made until all arrangements for obtaining the IND and the agent are completed. Final awards will also consider not only the cost of the clinical trial but also the cost of the agent and, if necessary, its formulation.

#### FUNDS AVAILABLE

Approximately \$4.0 million in total costs per year for five years will be committed to specifically fund applications which are submitted in response to this RFA. It is anticipated that 9 to 15 awards will be made annually. This number of awards is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications submitted in response to the present RFA should not exceed five years. The earliest feasible start date for the initial awards will be December 1993. Although this program is provided for in the financial plans of the NCI, awards made pursuant to this RFA will be contingent upon the continued availability of funds for this purpose.

#### RESEARCH OBJECTIVES

This RFA encourages submissions of applications from investigators wanting to conduct collaborative translational research in cancer chemoprevention. Translational research moves the results of basic research studies in the laboratory or developmental studies to clinical research in human subjects or populations. The research objectives of these projects should be the development of intermediate biomarkers of cancer risk and the evaluation of the efficacy of individual biological and/or molecular markers as intermediate endpoints in chemoprevention trials.

Candidate chemical, biological, molecular, and dietary cancer chemopreventive agents have been identified from in vivo studies in animal model systems, and epidemiological studies. The efficacy of each of these agents individually or in concert in modulating cancer risk can best be evaluated through prevention clinical trials. Limitations of the usefulness of such trials is the long duration and large sample populations generally needed to achieve statistical significance. This limitation could be overcome by identification of biological or molecular markers suitable for use as intermediate endpoints in the process of carcinogenesis. Ideally, such markers would be expressed in an abnormal form in tumor tissue or washings or in serum of high-risk individuals, but revert to the normal form when exposed to the chemopreventive agent.

Our evolving understanding of the molecular biology of carcinogenesis has identified possible oncogene and suppressor gene candidates and molecular alterations in these candidates and their interactions with other cellular components, that could serve as intermediate markers in cancer chemoprevention trials. Examples would include sequential genetic alterations in oncogenes HER-2/neu, C-myc, c-abl; in tumor suppressors RB, p53 and APC; markers for increased risk for cancer (Li-Fraumeni-p53, NF-1, APC, and early onset 17q21); and interactions between oncogenes, suppressor genes and the cyclin P34 complex. New developments in the understanding of cellular function and metabolites have provided information on possible candidate markers for cell growth, proliferation, differentiation, and neoplastic transformation. Included among these candidates are abnormal cytology, nuclear aberrations (micronuclei), ornithine decarboxylase and/or prostaglandins synthetase, DNA ploidy, and colonic mucosal proliferation.

Cancer chemoprevention trials responsive to this RFA will examine modulation of candidate markers in response to administration of chemopreventive agents. Additionally, these markers could be used to identify human populations at high risk for cancer, and therefore useful as sample populations for these trials.

#### SPECIAL REQUIREMENTS

This RFA represents a single competition, with a specified deadline, February 9, 1993, for receipt of applications. It is expected that each application will describe plans for a mixture of basic, developmental and clinical research from an investigator wanting to focus on a particular study in cancer chemoprevention. Each application should have a general focus on study outcomes, and on the application of basic research and development to human subjects and populations.

If not contained within the investigator's own research project, plans should be cited for establishing contacts with investigators with complementary interests that would fulfill the broader goals of transitional chemoprevention studies.

All PHS and NIH grant policies will apply to applications received in response to this announcement.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study population for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by December 9, 1992, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NCI staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to Dr. Marjorie Perloff at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these cooperative agreements. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, Maryland 20892, telephone 301/496-7441; and from the NCI Program Director named below.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, exact, clear, single-sided photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At time of submission, two additional copies of the application must also be sent to:

Referral Officer  
Division of Extramural Activities  
National Cancer Institute  
Room 848, Westwood Building  
5333 Westbard Avenue  
Bethesda, MD 20892

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed (initially) by the DRG for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the RFA is an NCI program staff function. Applications will be judged to determine if they meet the goals and objectives of the program as described in the RFA. Applications that are judged non-responsive will be returned to the applicant, but may be submitted for investigator initiated grant competition at the next receipt date. Questions concerning the relevance of proposed research to the RFA may be directed to the NCI Program Director listed under INQUIRIES.

If the number of applications is large compared to the number of awards to be made, the NCI may conduct a preliminary scientific peer review to identify those which are clearly not competitive for awards.

Those applications judged to be both competitive and responsive will be further evaluated, using the review criteria shown below, for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board considers the special needs of the Institute and the priorities of the National Cancer Program.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Marjorie Perloff, M.D.  
Chemoprevention Branch  
National Cancer Institute  
Executive Plaza North, Suite 201  
Bethesda, MD 20892-4200  
Telephone: (301) 496-8563  
FAX: (301) 402-0553

Direct inquiries regarding fiscal matters to:

Ms. Eileen Natoli  
Division of Cancer Prevention and Control  
Grants Administration Branch  
National Cancer Institute  
Executive Plaza South, Suite 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800 Ext. 56

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 301 (Public Law 78-410; 42 U.S.C. 241, and Section 412, as amended by Public Law 99-158, 42 U.S.C. 258a-1); and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## VANADIUM SALTS IN THE CLINICAL TREATMENT OF DIABETES MELLITUS

NIH GUIDE, Volume 21, Number 42, November 20, 1992

RFA AVAILABLE: DK-93-11

P.T. 34; K.W. 0715075, 0740020, 0755015, 0765020, 1007009

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: February 18, 1993

Application Receipt Date: March 17, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

## PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites investigator-initiated research grant applications to study the effects of vanadium salts as potential therapeutic agents for the treatment of diabetes mellitus. A significant amount of prior research in experimental animals, isolated tissues, and cell preparations has strongly suggested that various forms of vanadium have a beneficial impact on the abnormal metabolic state associated with this disease. This solicitation intends to support preliminary studies of efficacy, dosimetry and toxicity in human subjects with diabetes.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Vanadium Salts in the Clinical Treatment of Diabetes Mellitus, is related to the priority area of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit or nonprofit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Minority individuals and women are encouraged to submit as Principal Investigators.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed two years. The anticipated award date is September 30, 1993.



This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

In order to adhere to prudent principles of cost-containment, requested direct costs must not exceed \$160,000 for any single application. Applications exceeding this limit will not be reviewed as part of this RFA. With respect to post-award administration, the current policies and requirements that govern the research grant programs of the NIH will prevail.

#### FUNDS AVAILABLE

A total of up to \$500,000 for first year expenses and \$500,000 for second year expenses will be committed by the NIDDK to fund applications submitted in response to this RFA. The NIDDK plans to make one to three awards in FY 1993 contingent on the receipt of highly meritorious applications in response to this solicitation. The award of grants pursuant to this RFA is contingent on the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

Vanadium, a trace metal for a broad range of organisms including humans, has been postulated to be a co-factor for a number of enzymatic processes. Salts of this element have been known for a decade to inhibit the action of a number of phosphatases in *in vitro* situations. In particular, vanadate has been used frequently in laboratory settings with isolated tissues and cell cultures as a tool in biochemical studies of the mechanisms of insulin action and experimental insulin resistant states. This ion has shown insulinmimetic properties in preparations of muscle, liver and adipose tissue as well as whole animals with various forms of diabetes. Non-diabetic laboratory animals appear to show much less response.

Despite the lack of consensus on the precise biochemical mechanism of action for vanadate, it is clear that a broad array of cellular and physiologic processes are modified in an insulinmimetic pattern. The magnitude and universality (i.e., across tissues, across species, across diabetes type or model) of these effects are still being debated in the literature. In addition, vanadium can exist in a number of oxidation states (both cationic and anionic), and the state most relevant to insulin action is not established.

Before embarking on human studies, it will be important to consider the known and potential toxicities of vanadium. Clinical studies of any vanadium compound with regard to diabetes will need to carefully monitor for incipient toxicity.

The objective of this RFA is to stimulate investigator-initiated research designed to provide feasibility data on the clinical utility of vanadium-containing compounds for the treatment of diabetes mellitus in humans. Therefore, all applications in response to this RFA must primarily concern the clinical study of patients with this disease (NIDDM and/or IDDM) and may include normal (non-diabetic) volunteers as appropriate to the experimental design.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Potential applicants are strongly encouraged to submit a letter of intent by February 18, 1993. The letter of intent is to include: (1) names of the Principal Investigator/program director and principal collaborators, (2) descriptive title of the potential application, (3) identification of the organization(s) involved, and (4) the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIDDK staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083  
FAX: (301) 402-1277

#### APPLICATION PROCEDURES

Applications must be received by March 17, 1993. Additional information about application procedures and appropriate forms is provided in the RFA.

#### REVIEW CONSIDERATIONS

Applications in response to this solicitation will be reviewed using the usual NIH peer review procedures. For further details, applicants are referred to the RFA document.

## INQUIRIES

Inquiries regarding programmatic issues related to this announcement and requests for the RFA may be directed to:

Joan T. Harmon, Ph.D.  
Executive Director, Diabetes Research Program  
Diabetes Programs Branch, DDEM  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 622  
Bethesda, MD 20892  
Telephone: (301) 496-7731  
FAX: (301) 480-0383

Inquiries regarding fiscal matters may be directed to:

Betty Bailey  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467  
FAX: (301) 496-9721

## Schedule:

Letter of Intent:	February 18, 1993
Application Receipt Date:	March 17, 1993
Initial Review:	June/July 1993
NIDDK Advisory Council Review:	September 1993
Anticipated Award Date:	September 30, 1993

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.847. Awards are made under the authority of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## EFFECTS OF SEX HORMONES ON CORONARY ARTERY REACTIVITY

NIH GUIDE, Volume 21, Number 42, November 20, 1992

RFA AVAILABLE: HL-93-05-H

National Heart, Lung, and Blood Institute

P.T. 34; K.W. 0715040, 0760025, 0760085, 1002061, 0765035

Letter of Intent Receipt Date: February 1, 1993  
Application Receipt Date: April 27, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

## PURPOSE

The Division of Heart and Vascular Diseases invites grant applications for up to five years of support for research into the roles of sex hormones in the physiology and pathophysiology of the coronary vasculature. The ultimate goal is to develop insights into therapeutic approaches for reducing the higher incidence of coronary diseases in men and post-menopausal women than pre-menopausal women.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Effects of Sex Hormones on Coronary Artery Reactivity, is related to the priority area of heart disease and stroke. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for each application submitted in response to the present RFA may not exceed five years. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

#### FUNDS AVAILABLE

Approximately \$1.5 million in total cost will be provided for the first year of support for the entire program. It is anticipated that six new grants will be awarded under this program. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the National Heart, Lung, and Blood Institute (NHLBI), awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Administrative adjustments in project period and/or amount of support may be required at the time of the award. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded.

#### RESEARCH OBJECTIVES

Recent studies reveal that temporary ischemia can occur, not only as a result of organic obstruction of the coronary artery, but also as a result of vasoconstriction and vasospasm. Added to this is the fact that gender is one of the major risk factors for the development of coronary artery disease. Involvement of sex hormones in vascular reactivity has been suggested frequently, but clear evidence for a mechanism is lacking. Gender differences in vascular reactivity have been demonstrated by several research groups, and these studies have demonstrated that coronary vessels from male animals show greater vascular reactivity. However, the degree to which coronary smooth muscle and the endothelium are sexually differentiated and modulated by sex hormones remains to be determined.

It has been suggested that one of the protective effects of estrogens may involve influences on structural elements of the vessel wall. However, no attempt has been made to see whether or not there is a sex difference in the distribution and density of steroid binding sites. Furthermore, a correlation between steroid hormone receptors and hormonal modulation of cell function in the coronary vasculature still needs to be determined. The role of coronary reactivity should be evaluated in mature and immature animals of both sexes in terms of its morphological, pharmacological, and biophysiiochemical characteristics.

Sex hormones interact with the sympathetic nervous system at the peripheral level, suggesting that sympathetic control of vascular reactivity exhibits a dimorphic pattern due to the action of sex hormones. Physiological stress such as exercise and hypoxia increases the sympathetic activity of the heart. Whether or not the coronary vascular bed responds to these stimuli in a sexually differentiated manner is still unclear. An evaluation of the interaction between the sympathetic nervous system and sex hormones in this specific vascular bed will certainly provide important information regarding the mechanisms underlying coronary vascular disease under normal and stressful conditions in men and women across all ages.

All applications must be focussed on the role of the sex hormones in coronary reactivity. The spectrum of experimental approaches considered responsive to this RFA includes in vivo and in vitro studies of coronary vascular reactivity, co-culture techniques to elucidate cell to cell interaction, cell receptor density, as well as molecular pharmacological approaches that will enhance our understanding of how sex hormones regulate coronary vascular cell function.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by February 1, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NHLBI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Chief, Centers and Special Projects Section, Review Branch  
Division of Extramural Affairs  
National Heart, Lung and Blood Institute  
Westwood Building, Room 553A  
Bethesda, MD 20892

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and may be obtained from the Office of Grants

Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

Send or deliver a signed, typewritten original of the application, including the checklist, and three signed photocopies to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Send two additional copies of the application to the Chief, Centers and Special Projects Section, at the address listed under LETTER OF INTENT.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or principal investigator could be included with the application.

Applications must be received by April 27, 1993.

#### REVIEW CONSIDERATIONS

Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NHLBI. The second level of review will be provided by the National Heart, Lung, Blood Advisory Council.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications. Although multidisciplinary approaches are encouraged, it is not the intent of this announcement to solicit applications for large studies that would encompass a variety of independent projects, i.e., program projects.

#### AWARD CRITERIA

The most important criterion in selecting awardees will be the scientific merit as reflected in the priority score. However, factors such as program balance and available funds may enter into selection from among meritorious applications.

The anticipated date of award is December 1, 1993.

#### INQUIRIES

Inquiries regarding programmatic issues and requests for the RFA document to:

Dr. Isabella Liang  
Division of Heart and Vascular Diseases  
National Heart, Lung and Blood Institute  
Federal Building, Room 3C06  
Bethesda, MD 20892  
Telephone: (301) 496-1081  
FAX: (301) 480-6282

Direct inquiries regarding fiscal and administrative matters to:

Mr. William Darby  
Division of Extramural Affairs  
National Heart, Lung and Blood Institute  
Westwood Building, Room 4A11  
Bethesda, MD 20892  
Telephone: (301) 496-7536  
FAX: (301) 402-1200

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency Review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### DRUG ABUSE TREATMENT OF CRIMINAL JUSTICE-INVOLVED POPULATIONS

NIH GUIDE, Volume 21, Number 42, November 20, 1992

PA AVAILABLE: PA-93-21

P.T. 34; K.W. 0404009, 0404000, 0745070, 0403004

National Institute on Drug Abuse



THE PROGRAM ANNOUNCEMENT ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE PROGRAM ANNOUNCEMENT FROM THE CONTACTS NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The purpose of this announcement is to encourage research on models of intervention for drug abusers involved with the criminal justice system (CJS). Applications may focus on drug abuse treatment linked to the criminal justice system which is delivered prior to or in lieu of incarceration, during the period of incarceration, after release, or in combinations of these. Applications are also sought for community-based outreach/intervention behavioral change strategies in the population of criminal-justice-involved drug users not in treatment.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000", a PHS-led national activity for setting priority areas. This announcement, Drug Abuse Treatment of Criminal Justice-Involved Populations, is related to the priority area of health promotion/alcohol and other drugs. Some applications under this announcement may also be related to the priority area of health promotion/violent and abusive behavior. Potential applicants may obtain a copy of Healthy People 2000 (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit, public and private organizations such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Women and minority investigators are encouraged to apply. Applications are especially encouraged from State and municipal governments with research units and/or State and municipal governments collaborating with university-based research units.

#### MECHANISM OF SUPPORT

This Program Announcement will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Support will be provided for a period of up to five years (renewable for subsequent periods) subject to continued availability of funds and progress achieved. Because of the nature and scope of the research proposed in response to this program announcement may vary, it is anticipated that the size of an award will vary also.

#### RESEARCH OBJECTIVES

##### Summary

Carefully controlled research studies are sought to investigate the effectiveness and cost-effectiveness of drug abuse treatment linked to criminal justice system involvement and delivered (1) prior to or in lieu of prosecution or incarceration; (2) in the jail or prison setting during the period of incarceration; (3) after release or during transition from incarceration to release; or (4) for combinations of these. Research studies to investigate community-based outreach/intervention behavioral change strategies in the population of criminal-justice-involved drug users not in treatment will be supported. Of particular interest are research projects in geographic areas having a high or unmet need for drug treatment services in the criminal justice-involved population.

##### Program Description

Applicants are advised to review existing information relevant to drug abuse treatment of CJS-involved populations and to design controlled clinical studies to determine the impact of providing drug abuse treatment to CJS-involved clients. Areas of research interest include the following:

##### General

- o Improvement of treatment outcomes for individuals under legal sanction.
- o Joint effects of criminal justice sanctions and treatment.
- o Strategies to increase retention, improve participation in treatment, and reduce relapse to drug use and recidivism to criminal activity.
- o Effectiveness of drug abuse treatment intervention strategies for the drug-abusing juvenile offender.

##### Pre-Incarceration

- o Characterization and assessment of criminal justice clients most likely to benefit from drug abuse treatment.
- o The effectiveness of matching criminal justice clients to appropriate treatment.
- o Effectiveness of treatment in lieu of prosecution/incarceration in reducing drug use, reducing criminal behavior, and increasing productive activities.
- o Effect of legal pressure on client treatment compliance and outcome variables. For example, does drug testing increase compliance with treatment or improve outcomes?

## Institution-Based

- o Effectiveness and cost-effectiveness of institution-based treatment approaches, including effectiveness of treatment beyond the period of incarceration, and strategies to maintain and increase treatment gains after return to the community.
- o Increasing the effectiveness of treatment delivered early in an individual's period of incarceration.
- o Overcoming barriers to implementation of effective treatment within the institutional setting, and effect of institutional incentives and disincentives on treatment outcomes.
- o Relationship of inmate characteristics and criminal backgrounds to treatment compliance and outcomes.

## Post-Incarceration

- o Improvement of the effectiveness of drug abuse treatment and aftercare in halfway houses and similar transitional programs charged with re-integrating former inmates into the community.
- o Effectiveness of treatment after release compared with non-treatment alternatives such as intensive supervision and monitoring, parole supervision, and release without supervision.
- o Treatment program and client factors which predict relapse to illicit drug use and recidivism to drug-related criminal activity.

## Community-Based

- o Community-based outreach/intervention behavior change strategies, especially in out-of-treatment individuals, to reduce illicit drug use and drug-related risks such as HIV, TB, STDs, and re-involvement in the criminal justice system/process.
- o Efficacy of community-based outreach/intervention strategies to improve health and to reduce drug use and criminal behavior among youth and adults at different stages of involvement in the criminal justice system/process.

The importance of a sound research plan and qualified research staff cannot be over-emphasized. It is recommended that investigators use the most rigorous methodology consistent with the purposes of the research. Where controlled trials are not feasible, other types of controls may be used, including case controls, equivalent comparison groups, regression-discontinuity, or other designs. While many treatment or criminal justice agencies have a research department, those that do not may wish to enter into collaboration with well-qualified researchers. All applications are strongly encouraged to address issues of project feasibility and collaborative arrangements, study design, sampling procedures, implementation of the intervention, instrumentation and measurement, data collection, quality control, tracking of clients, followup, and data analysis, as appropriate.

Investigators are encouraged to offer HIV testing and counseling in accordance with current guidelines to subjects identified during the course of the research as being at risk for HIV acquisition or transmission. In high risk populations, investigators are encouraged to assess the effects of new interventions on the acquisition and transmission of infectious diseases, including HIV.

## STUDY POPULATIONS

### NIH POLICY CONCERNING INCLUSION OF MINORITIES AND WOMEN AS SUBJECTS IN RESEARCH

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

### Human Subjects Protections for Research Involving Prisoners

Activities carried out under this announcement may be governed by DHHS Regulations for the Protection of Human Research Subjects (45 CFR 46). These regulations require awardees to establish procedures for the protection of human subjects involved in any research activities. Projects involving prisoners require special additional protections in accordance with Subpart C of the DHHS regulations.

Prior to funding and upon request of the Office for Protection from Research Risks (OPRR), prospective awardees not holding an OPRR-approved Multiple Project Assurance must file a Single Project Assurance with OPRR and establish or identify an Institutional Review Board (IRB) to review and approve the procedures for carrying out any human subjects research occurring in conjunction with this award. A formal request for the required Assurance will be issued by OPRR at an appropriate point in the review process, and examples of required materials will be supplied at that time. However, applicants may wish to contact OPRR (301-496-7041) to obtain preliminary guidance on human subjects issues. When calling OPRR, applicants should identify themselves as having questions about research involving prisoners.

## APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions.

Application kits are available at most institutional offices of sponsored research and may be obtained from the

Office of Grant Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 240, 5333 Westbard Avenue, Bethesda, Maryland 20892, telephone 301-496-7979. The title and number of the announcement must be typed in Section 2a on the face page of the application.

The completed original and five permanent, legible copies of the PHS 398 form must be submitted to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

The Division of Research Grants, NIH, serves as a central point for receipt of applications for most discretionary DHHS grant programs. Applications received under this announcement will be assigned to an initial review group (IRG) in accordance with established PHS referral guidelines. The IRGs, consisting primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit in accordance with the standard NIH peer review procedures. Notification of the review recommendations will be sent to the applicant after the initial review. Applications will receive a second-level review by an appropriate Advisory Council, whose review may be based on policy considerations as well as scientific merit. Only applications recommended for further consideration by the Council may be considered for funding.

#### AWARD CRITERIA

Applications recommended for further consideration by an appropriate Advisory Council will be considered for funding on the basis of overall scientific, clinical and technical merit of the proposal as determined by peer review, appropriateness of budget estimates, program needs and balance, policy considerations, adequacy of provisions for the protection of human subjects, and availability of funds.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues related to treatment research to:

Bennett W. Fletcher, Ph.D.  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 10A-30  
Rockville, MD 20857  
Telephone: (301) 443-4060

Direct inquiries regarding programmatic issues related to community-based behavioral change research to:

Richard H. Needle, Ph.D., M.P.H.  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 9A-30  
Rockville, MD 20857  
Telephone: (301) 443-6720

Direct inquiries regarding fiscal matters to:

Ms. Shirley Ann Denney  
Grants Management Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.279. Awards are made under authorization of the Public Health Service Act, Sections 301 and 405 (42 USC 241 and 284), and administered under PHS grants policies and Federal Regulations at 42 CFR 52, 45 CFR Part 74 & 92, and 45 CFR Part 46. 42 CFR Part 2 may also be applicable to these awards. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### "FAILURE TO THRIVE" SYNDROME AMONG OLDER PERSONS

NIH GUIDE, Volume 21, Number 42, November 20, 1992

PA: PA-93-22

P.T. 34; K.W. 0710010, 0710095, 0715072, 0710070, 0765035

National Institute on Aging  
National Institute of Mental Health

#### PURPOSE

Recently, a geriatric syndrome termed "failure to thrive" has been described, consisting of weight loss,

NIH Guide for Grants and Contracts - Vol. 21, No. 42 - November 20, 1992



decreased appetite, poor nutrition, and inactivity, often accompanied by dehydration, depressive symptoms, impaired immune function, and low serum cholesterol. Failure to thrive occurs in both acute and chronic forms, leading to impaired functional status, morbidity from infection, pressure sores, and increased mortality. This syndrome has been identified as an aging research priority in the Institute of Medicine's report: *Extending Life, Enhancing Life. A National Research Agenda on Aging.* (Institute of Medicine; National Academy Press, Washington, 1991.) The relationships between nutritional, metabolic and other pathophysiologic factors in failure to thrive and their effects on clinical outcomes remain to be clarified. While there is evidence that psychiatric conditions (major and subsyndromal depression and cognitive decline) are frequently associated with failure to thrive, the nature of this association needs to be clarified.

"Failure to thrive" in older persons may not be a single process. It may be caused by several different pathophysiologic processes. Thus there is a strong need for descriptive information on the progression of failure to thrive in various specific groups of older persons with different chronic diseases and disabilities, to elucidate potential differences and commonalities in pathophysiologic mechanisms and clinical course.

The relationship between nutritional, metabolic and other pathophysiologic mechanisms in failure to thrive, and their effects on clinical outcomes, remains to be clarified. Numerous studies have documented the extent of protein-calorie malnutrition among nursing home residents and other specific older populations. In addition, it has been suggested that micronutrient deficiencies may play a larger role in chronic debilitating changes in older persons than is currently appreciated. Alterations in endocrine factors affecting metabolism, inflammatory mediators, and depressive changes in affect have also been suggested to play a major role in failure to thrive. The contribution of specific chronic disease processes and acute conditions to failure to thrive has yet to be explored fully. The effectiveness of interventions against failure to thrive and loss of appetite in older persons has not been rigorously tested.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), "Failure to Thrive" Syndrome Among Older Persons, is related to the priority area of aging. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-00473-1) through the superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, unit of state and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) awards (R29) or for the Career Awards (K01, K04, K07, K08, K11, K20, K21).

#### MECHANISM OF SUPPORT

Awards will be administered under PHS grants policy as stated in the Public Health Service Grants policy statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990. The National Institute on Aging (NIA) intends to commit \$1.8 million in Fiscal Year 1994 for this research area. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Applications in response to this announcement assigned to the NIA may not request funding over \$175,000 (direct and indirect costs) for the first year, and may not request more than four percent per year above \$200,000 for subsequent years. Additionally, the National Institute of Mental Health (NIMH) anticipates supporting approximately 4-6 awards under this announcement. The Principal Investigators will meet annually with NIA and NIMH staff in Bethesda, Maryland to review the progress of their studies. Funds for such travel must be requested in applications.

The mechanisms for support are:

- o Research Grant (R01)
- o FIRST award (R29)
- o Career awards, which include: Special Emphasis Research Career Awards (K01) in Nutritional and Metabolic Factors in Aging, Research Career Development Award (K04), Clinical Mental Health Academic Award (K07), Clinical Investigator Award (K08), Physician Scientist Award (K11), Scientist Development Award for Clinicians (K20), and Scientist Development Award (K21)

#### RESEARCH GOALS AND SCOPE

The NIA seeks applications for support of research to clarify pathophysiological features of the "failure to thrive" syndrome in older persons and research into its causes, prevention, and treatment. Topics of interest include:

- o Risk factors, natural history, clinical, and functional features of failure to thrive in various high-risk older subpopulations. Though large scale primary epidemiologic studies are outside the scope of this PA, ancillary studies to existing population studies are appropriate and encouraged.
- o Primary endocrine, metabolic, cellular and related pathophysiologic mechanisms contributing to failure to thrive in older persons.
- o Relationship between nutritional deficiencies, or impairments in nutrient disposition or metabolism, as causes or results of the various pathophysiological abnormalities described in "failure to thrive" in older persons.



- o Interactions and interrelationships among the different components of failure to thrive, e.g. hypcholesterolemia, specific abnormalities in immunologic and inflammatory factors, infection, depression.
- o Metabolic responses and alterations in nutritional needs of older persons associated with acute conditions that may provoke failure to thrive, e.g., infections, trauma, or surgery.
- o Factors modulating control of appetite as a cause or consequence of failure to thrive.
- o Pathophysiologic effects of coexisting chronic diseases and/or comorbid processes of aging contributing to failure to thrive.
- o The role of psychosocial and cultural factors, (e.g., social supports, social stressors, bereavement, depression, mood and affect, cultural preferences) in failure to thrive syndrome.
- o Development and use of appropriate animal models for studying failure to thrive in older persons.
- o Neural interactions with physiological processes underlying failure to thrive syndrome.
- o Efficacy of interventions in preventing, arresting, or reversing failure to thrive. Applicants may choose to study specific populations and conditions, e.g., post-surgical or trauma patients, infections, or depression. Attention to physiologic factors or comorbid conditions modulating efficacy of interventions in these conditions is particularly encouraged.
- o Delineation of psychiatric conditions of failure to thrive (including the range of clinically significant affective symptoms) and the elucidation of the interrelationship among psychiatric status, physiological measures, and behavior.

For any of the above topics, attention to the heterogeneity and frequent multiple morbidity within the geriatric population is encouraged in the design of research projects.

#### STUDY POPULATIONS

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them. The study design must seek to identify any pertinent gender or minority population differences.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that, as appropriate, applicants for NIH grants, cooperative agreements, and contracts will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the diseases, disorders, or conditions under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders, and conditions that disproportionately affect them. This policy is intended to apply to males as well as females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale for exception to the policy must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic groups, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives, Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority populations should be provided. For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are exempt. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants. For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned without review.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study is inadequate to answer the scientific questions(s) addressed and the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application. All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

## APPLICATION PROCEDURES

Applications are to be submitted on the application form PHS 398 (rev. 9/91) available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone 301/496-7441. Applications will be accepted on the standard application receipt dates as indicated in the application kit. The program announcement title and number must be typed on line 2a of the face page.

The completed original application and five legible copies must be sent or delivered to:

Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

## REVIEW PROCEDURES

Applications will be reviewed by the NIH Division of Research Grants (DRG). The review criteria are the traditional considerations underlying scientific merit. Applications will be reviewed by standard NIH review procedures in accordance with the usual NIH peer review procedures, based on scientific merit. Following study section review, the applications will be evaluated by the appropriate national advisory council.

The review criteria for each mechanism may be obtained from the program contact listed below.

## AWARD CRITERIA

Applications will compete for available funds on the basis of scientific merit with other applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

## INQUIRIES

The opportunity to clarify any issues and questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Pamela Starke-Reed, Ph.D., Geriatrics Program, Suite 3E327  
Telephone: (301) 496 6761

Huber Warner, Ph.D., Biology of Aging Program, Suite 2C231  
Telephone: (301) 496-6402

Marcia Ory, Ph.D., M.P.H., Behavioral and Social Research Program, Suite 2C234  
Telephone: (301) 496-3136

Andrew Monjan, Ph.D., Neuroscience and Neuropsychology of Aging Program, Suite 3C307  
Telephone: (301) 496-9350

All are at the NIA with the following address:

National Institute on Aging  
Gateway Building  
Bethesda, MD 20892

or

Rick Martinez, M.D. or Enid Light, Ph.D.  
Mental Disorders of the Aging Research Branch  
National Institute of Mental Health  
5600 Fishers Lane, Room 7-103  
Rockville, MD 20857  
Telephone: (301) 443-1185

Direct inquiries regarding fiscal matters to:

Barbara Cunningham  
Grants and Contracts Management Office  
National Institute on Aging  
Gateway Building, Room 2N212  
Bethesda, MD 20892  
Telephone: (301) 496-1472

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410), as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and

#### HEMOGLOBIN-BASED OXYGEN CARRIERS: MECHANISMS OF TOXICITY

NIH GUIDE, Volume 21, Number 42, November 20, 1992

PA: PA-93-23

P.T. 34; K.W. 0785070, 1003002, 1002004, 1002008, 0710100, 0765035

National Heart, Lung, and Blood Institute

#### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) announces a Program Announcement (PA) on the above subject. The purpose of this initiative is to encourage research aimed at providing an understanding of the mechanisms of toxicity of hemoglobin-based oxygen carriers.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Hemoglobin-based Oxygen Carriers: Mechanisms of Toxicity, is related to the priority area of food and drug safety. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-782-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged. Awards in connection with this announcement will be made to foreign institutions only for research of very unusual merit, need and promise, and in accordance with PHS policy governing such awards. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards.

#### MECHANISM OF SUPPORT

This PA will use the National Institutes of Health (NIH) research project grant (R01) and FIRST (R29) award. Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project. Up to five years of support may be requested. Because the nature and scope of the research proposed in response to this PA may vary, it is anticipated that the size of an award will also vary. Those applicants requesting support under the FIRST (R29) award should be certain that the direct costs requested are within the guidelines for that award. Administrative adjustments in project period and/or amount of support may be required at the time of the award. All current policies and requirements that govern the research grant programs of the NIH will apply to grants awarded in connection with this PA.

#### RESEARCH OBJECTIVES

##### Background

An alternative to red blood cells for transfusion has been sought unsuccessfully for over one hundred years. In recent years, the NHLBI and other government agencies have supported research on the development of stable oxygen carriers that do not need to be cross-matched and that can be stored for extended periods of time. During the past decade, awareness of the dangers inherent in transfusion of homologous red blood cells has heightened. These include transmission of infectious agents such as HIV, hepatitis viruses and other microorganisms. Consequently, physicians are increasingly reluctant to transfuse their patients and patients are increasingly reluctant to receive blood. Although testing of units of blood is becoming more comprehensive and efficient, there is no question that products that are free of infectious agents that could be used in place of red cells would have wide clinical application. In spite of this promise, studies of hemoglobin-based oxygen carriers have been disappointing as unpredictable toxicities have thwarted development of clinically useful products.

Infusion of hemoglobin-based oxygen carriers into the circulation can result in a variety of outcomes. Carrier molecules may leave the circulation by a number of routes including endothelial transcytosis, phagocytic uptake, and diffusion. The effects of these materials may be as diverse as the range of properties of the various tissues they bathe. Their interaction with endothelium-derived relaxing factors, stimulation of other vasoactive materials, and stimulation of mediators of inflammation may add to the complex biological reactions noted in research to date. Furthermore, much of the previous work in this field is clouded by species differences, so that, at present, there are no animal or in vitro models that will reliably predict human reactions.

In addition to Federal support, research and development of artificial oxygen carriers have been carried out by industry. Indeed, industry has contributed valuable knowledge in the area of product and quality control. Sophisticated high technology systems have been developed to produce products in large quantities. However, in recent clinical trials with hemoglobin-based oxygen carriers, unexpected toxicities were observed suggesting the need for more basic research to address fundamental questions concerning interaction with the immune system and endothelium in particular.



The purpose of this PA is to encourage research aimed at providing an understanding of the mechanisms of toxicity of hemoglobin-based oxygen carriers. This program encourages research addressing such fundamental questions as: (1) what are the mechanisms of vasoactivity of hemoglobin solutions, (2) how do protein modifications affect vasoactivity, (3) what are the mechanisms of stimulation of inflammation mediators by hemoglobin-based oxygen carriers, (4) how can this stimulation be prevented, (5) what animal or in vitro models are best used to study toxic effects of oxygen carriers, (6) what are the long-term (metabolic and pharmacologic) effects of oxygen carriers, and (7) what models are best to demonstrate efficacy in terms of oxygen transport to tissue. Particular encouragement is offered to investigators possessing modern tools, who are well-trained, and who are currently pursuing other research interests to devote time and resources to this area. It is hoped that interdisciplinary and collaborative approaches may be developed which will complement the efforts of workers in the field. The ultimate goal is to satisfy a fundamental need in clinical medicine, i.e., development of a safe, economical and efficacious alternative to homologous human red blood cells for transfusion.

Examples of promising topics are:

- o Studies of the interaction of hemoglobin with endothelium and macrophages.
- o Development of animal models that simulate clinical use, such as trauma, shock, infection, and surgical blood loss.
- o Studies relating the biochemical modification of hemoglobin with its biological effects.
- o Studies of encapsulation of hemoglobin into artificial vesicles - biochemical, physical, physiological, and biological effects.
- o Studies of the tissue distribution and metabolic fate of modified hemoglobins, and artificial vesicles.

These are intended as examples only. Investigators are encouraged to consider other innovative approaches.

Applications may address one or several issues, but should retain a common theme and focus on addressing those issues. Because issues involving hematology, biochemistry, physiology, cell biology, pharmacology or molecular biology may need to be addressed in a coordinated manner, collaboration among investigators having expertise in these and other appropriate disciplines is encouraged. When individuals are at different institutions, individual R01 applications may include consortium arrangements.

While the main focus of this PA is on basic or fundamental research studies to elucidate the mechanisms of toxicity of hemoglobin-based oxygen carriers, clinical studies, but not clinical trials, are also appropriate. Collaborative arrangements with ongoing clinical studies or trials that provide patient material at little or no cost to the applicant are also encouraged. Such arrangements should be clearly delineated in the application. The description should include sufficient information to permit scientific evaluation of the studies proposed. Among issues to include are the number and type of specimens/patients, patient population characteristics (including gender and minority composition; see STUDY POPULATIONS below), overall goals of the collaborative project, remaining term of the project, and IRB approval of the project. If substantial interactions and costs with ongoing projects are proposed, a consortium agreement can be developed and submitted to support this additional research aspect.

If statistical analysis is anticipated, the methodologies and personnel involved should be described in the application and evident in the study design.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans including American Indians or Alaskan Natives, Asian/Pacific Islanders, Blacks, and Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs



in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 (rev. 9/91) instructions.

FIRST award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. Section 2 on the face page of the application must be completed. Check "YES" to indicate the application is submitted in response to a program announcement. The title and program announcement number must be typed in Section 2a of the application as follows: "HEMOGLOBIN-BASED OXYGEN CARRIERS: MECHANISMS OF TOXICITY" PA-93-23.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW CONSIDERATIONS

Although this is an NHLBI PA, the National Institute of Environmental Health Sciences also has an interest in the subject matter of this PA. Applications will be assigned to the most appropriate Institute on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard peer review procedures.

Following scientific-technical review, the applications will receive a second-level review by the appropriate advisory council.

#### AWARD CRITERIA

Funding decisions will be made on the basis of scientific and technical merit of the proposed grant as determined by peer review, program needs, balance among research areas of the announcement, and the availability of funds.

Awards in response to this PA will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with PHS policy governing such awards.

#### INQUIRIES

Inquiries regarding this program announcement may be directed to:

Dr. George J. Nemo  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Federal Building, Room 504  
Bethesda, MD 20892  
Telephone: (301) 496-1537  
FAX: (301) 496-9940

For fiscal and administrative matters, contact:

Ms. Jane R. Davis  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A15  
Bethesda, MD 20892  
Telephone: (301) 496-7257  
FAX: (301) 402-1200

The programs of the Division of Blood Diseases and Resources, NHLBI, are described in the Catalog of Federal Domestic Assistance No. 93.839. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or to Health Systems Agency review.

**VULNERABILITY OF THE OLFACTORY SYSTEM TO THE IMPACT OF ENVIRONMENTAL TOXICANTS AND PATHOGENS**

NIH GUIDE, Volume 21, Number 42, November 20, 1992

PA: PA-93-24

P.T. 34; K.W. 0705070, 1007003, 1007009, 1002030

National Institute on Aging  
National Institute of Allergy and Infectious Diseases  
National Institute on Deafness and Other Communication Disorders  
National Institute of Environmental Health Sciences  
National Institute of Neurological Disorders and Stroke

**PURPOSE**

The olfactory nerve provides a direct anatomic conduit between the external chemical environment and the brain. This location puts the olfactory system at risk for damage from environmental toxicants and pathogens. These toxic agents comprise the major health hazard to human olfaction. However, the direct and indirect effects of these agents on the peripheral and central olfactory system are poorly understood. The purpose of this Program Announcement (PA) is to foster investigator-initiated research fundamental to understanding the impact of environmental toxicants and pathogens on the olfactory system. A broad range of studies extending from the molecular to the behavioral areas of basic and clinical research is applicable to this PA. The scope of these areas encompasses the transport of toxic substances into the brain through the olfactory nerve; olfactory mucosal defense mechanisms; neurogenesis; the relation of neurodegenerative diseases, such as Alzheimer's disease, to olfactory abnormalities induced by toxic agents; and the vulnerability of an aged olfactory system to toxic agents.

**HEALTHY PEOPLE 2000**

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Vulnerability of the Olfactory System to the Impact of Environmental Toxicants and Pathogens, is related to the priority area of environmental health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-11474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-11473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

**ELIGIBILITY REQUIREMENTS**

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Applications from minority individuals and women are encouraged.

**MECHANISM OF SUPPORT**

The mechanisms available for the support of this program are research project grants (R01) and the First Independent Research Support and Transition (FIRST) (R29) awards. Foreign institutions are not eligible for FIRST (R29) awards.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources (NCRR) may wish to identify the GCRC as a resource for conducting the proposed research. If case, a letter of agreement from either the GCRC program director or Principal Investigator may be included with the application.

**RESEARCH OBJECTIVES**

**BACKGROUND**

Certain features of the olfactory system are valuable in the study of some general properties of neural systems and some of these features provide excellent models for studying the effects of environmental agents on sensory systems. For example, the vertebrate olfactory receptor neuron has become an important neurobiologic model system in the area of molecular and cell biology for the study of neuronal plasticity and neuronal development or neurogenesis, including the developmental steps of cell birth and lineage, differentiation, synaptogenesis, growth, migration, maturation, and death. The olfactory neuroepithelium is unrivaled in its capacity for neuron replacement and regeneration throughout life. Receptor neurons of the main olfactory system (and vomeronasal system) show a remarkable naturally occurring rate of turnover followed by functional synaptogenesis and are rapidly replaced following traumatic lesions. These are the only known projection neurons with this property. Molecular biologic studies have shown that the maturation process of regenerating olfactory receptor neurons involves the sequential expression of several growth associated proteins, such as olfactory marker protein. The robust ability of animals to detect and differentiate odorants has provided a valuable means to gauge the recovery of olfactory function with behavioral tests after damage to the receptor neurons.

The olfactory receptor neurons are extremely sensitive to chemical stimuli, exhibit specific ligand binding,

and are the only neurons that form a direct conduit between the external chemical environment and the brain. Uptake of even a small amount of a chemical substance by each olfactory receptor neuron could have an appreciable effect on the olfactory bulb because of the magnitude of the receptor neuron input to the bulb and the high degree of convergence of this input. These characteristics make the olfactory system vulnerable to damage from toxic agents; it has even been suggested that the very process of chemoreception is damaging to the olfactory receptor neurons. One of the most commonly used methods to study olfactory neurogenesis involves the destruction of certain cells in the olfactory neuroepithelium by chemicals, including toxicants such as methyl bromide. The development of tissue culture methods allows the pharmacologic manipulation of olfactory plasticity, neurogenesis, and interactions between the olfactory nerve and olfactory bulb.

The exposed location of the olfactory receptor neurons and their morphology make them exceptionally suitable for the study of axoplasmic transport. Marker substances and precursors can be applied to the nasal cavity without requiring surgery. The olfactory nerve consists of relatively homogeneous population of several million unmyelinated axons, only a minor fraction of the nerve volume being composed of glial cells and fibrocytes. Various organic and inorganic substances, including dyes, amino acids, colloidal gold, and lectins, can be taken up by the olfactory nerve and transported to the olfactory bulb. Videomicroscopic techniques are available to measure organelle movement during normal conditions and after pharmacologic manipulations.

The olfactory bulb is a model system for the study of neural organization and plasticity. For example, repeated stimulation of rat pups with a specific odorant appears to enhance bulbar neural responses and may induce a morphological rearrangement of the receptor axon terminals in the olfactory bulb. The olfactory bulb is well organized into distinct laminations that demarcate the local circuits. The neurons and synapses that make up these layers have been identified and well characterized. Further, the bulb is richly laden with a wide variety of neuroactive substances. These properties make the bulb an ideal physiologic preparation to localize drug and neurotransmitter receptors and to study the interactions of neurotransmitters with toxic substances. The recent application of voltage-sensitive dyes to the bulb allows simultaneous monitoring of odorant-evoked activity in many bulbar cells and permits clear interpretation of that activity. More recently, *in situ* hybridization has been used to study the effect of odor stimulation on *c-fos* mRNA expression in vertically distributed aggregates of bulbar neurons.

Several issues related to the impact of toxic agents on the olfactory system are mentioned below. A fundamental issue is the degree to which genetic and environmental factors affect human olfaction over the lifespan and regulate olfactory neurogenesis. Human olfactory function is known to decrease with age. Several studies in humans suggest that the olfactory mucosa is replaced with respiratory mucosa as a result of frequent infectious diseases of the nasal chambers, exposure to toxic chemicals, head injury, or age-related conditions. Continued mitosis in the olfactory neuroepithelium may be under the programmed genetic control of a biological clock. However, the longevity of an olfactory cell can be readily modified or manipulated by environmental factors, both in nature and in the laboratory.

Olfactory perireceptor events have also recently received attention. The identification of odorant binding proteins has generated interest in the influence of the composition and physical properties of olfactory mucus secretions on the access of odor molecules to receptor sites on olfactory receptor neurons, odorant binding, and clearance from the vicinity of these sites. The human olfactory mucosa is a site for synthesis and secretion of immune, antimicrobial, and other defense factors against pathogens. Although immunocytochemical studies have shown that the olfactory mucosa contains highly active enzyme systems, such as cytochrome P450, for metabolizing xenobiotics, including odorants, xenobiotic metabolism in the olfactory system has received little attention.

Issues regarding the transport of toxic agents into the olfactory system have important implications for public health. Some viruses are transported from the olfactory neuroepithelium to the olfactory bulb and then spread into the rest of the brain. According to some investigators, the olfactory deficits expressed in the early stages of Alzheimer's disease and Parkinson's disease may result from substances that entered the brain through the olfactory nerve. Some investigators have reported morphological and immunocytochemical abnormalities of the olfactory neuroepithelium in patients with Alzheimer's disease and Parkinson's disease.

The effects of environmental toxicants and pathogens on the olfactory system are complex and poorly understood. Studies of these effects are of great ecologic importance.

#### Research Goals and Scope

The ultimate goal of this research program to develop targeted drug delivery, vector-based vaccines, and other interventions for the treatment and prevention of the effects of toxic agents on the olfactory system. Collaboration is encouraged between investigators within and outside of the field of olfaction, including inhalation toxicologists, virologists, immunologists, and molecular biologists. A broad range of studies extending from the molecular to the behavioral levels of basic and clinical research is applicable to this Announcement. Topics might include some of those listed below. Investigators are encouraged to consider other topics relevant to this program.

- o For any suspected toxicant or pathogen, evidence of the causal relationship to observed findings of damage to the olfactory system.
- o Neurophysiologic and histopathologic studies that determine the localization of damage in the olfactory system.
- o Olfactory abnormalities induced by toxic agents as early signs of neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease.
- o Specific anosmias induced by toxic agents.
- o Age-related changes in chemosensory responses to toxic agents.



- o Investigations into the molecular mechanisms initiated by toxic agents.
- o Defense mechanisms of the olfactory system against the direct and indirect effects of toxic agents; the role of supporting cells in phagocytosis and other defense responses; and the role of Bowman's glands.
- o The role of xenobiotic metabolism in the peripheral and central olfactory system; biotransformation of a substance to a less or more toxic substance and biotransformation of a nonodorous substance into an odorous one; synergisms between toxic agents; and site-specific metabolism.
- o Active and passive mechanisms of uptake of toxic agents into the olfactory neuroepithelium.
- o Effects of toxic agents on stem cells and other cell populations of the olfactory neuroepithelium; neurogenesis of olfactory receptor neurons; trophic and tropic interactions between the olfactory nerve and the olfactory bulb; and olfactory bulb neurochemistry and glial cells.
- o Anterograde and retrograde axoplasmic transport of toxic agents in the olfactory nerve; impact of transport on neurogenesis; routing of proteins to specialized regions of the plasma membrane; and native mitochondrial synthesis and import of proteins in mitochondrial biogenesis.
- o Transneuronal transport of toxic agents from the olfactory bulb to other parts of the brain.
- o Comparison of the effects of toxic agents on olfaction with the effects on other chemosensory systems.
- o Interactions between the effects of nutrients and toxic agents on the olfactory system.
- o Mechanisms of regeneration, repair, or plasticity following administration of toxic agents; use of implantation of tissues to enhance these processes.
- o Development of more specific and sensitive tests for detecting early damage by toxic agents to the olfactory system; identification of naturally occurring models; and development of new animal models of neuronal regeneration and repair using paradigms involving damage to the olfactory system by toxic agents.
- o Potential of the olfactory nerve for administration of pharmacotherapeutics to combat the effects of toxic substances on the olfactory system.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS.

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities. If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room



449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in line 2a on the face page of the application.

FIRST award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original application and five exact copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by an appropriate national advisory council or board.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Program balance among research areas of the announcement
- o Availability of funds

#### INQUIRIES

Direct inquiries regarding the major areas of research interest in this program to:

##### Chemoreception

Jack Pearl, Ph.D.  
Division of Communication Sciences and Disorders  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400B  
Rockville, MD 20892  
Telephone: (301) 402-3464  
FAX: (301) 402-6251

##### Age-related disorders

Deborah L. Claman, Ph.D.  
Neuroscience and Neuropsychology of Aging  
National Institute on Aging  
Gateway Building, Suite 3C307  
Bethesda, MD 20814  
Telephone: (301) 496-9350  
FAX: (301) 496-1494

##### Infectious diseases

David Klein, Ph.D.  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3A10  
Bethesda, MD 20892  
Telephone: (301) 496-5305  
FAX: (301) 496-8030

##### Neurotoxicology of environmental toxicants/pollutants

Annette Kirshner, Ph.D.  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
Box 12233, MD 3-02  
Research Triangle Park, NC 27709  
Telephone: (919) 541-0488  
FAX: (919) 541-2860

##### Neural plasticity and axonal regeneration

Mary Ellen Michel, Ph.D.  
Division of Stroke and Trauma  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 8A13  
Bethesda, MD 20892

Telephone: (301) 496-4226  
FAX: (301) 480-1080

Direct inquiries regarding fiscal matters:

Sharon Hunt  
Division of Extramural Activities  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400B  
Rockville, MD 20892  
Telephone: (301) 402-0909  
FAX: (301) 402-1758



Joseph Ellis  
National Institute on Aging  
Gateway Building, Suite 2N212  
7201 Wisconsin Avenue  
Bethesda, MD 20814  
Telephone: (301) 496-1472  
FAX: (301) 402-0066

Todd Ball  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4835  
Bethesda, MD 20892  
Telephone: (301) 496-7075  
FAX: (301) 496-3780

Carolyn Winters  
Division of Extramural Research and Training  
National Institute of Environmental Health Sciences  
Box 12233, MD 2-01  
Research Triangle Park, NC 27709  
Telephone: (919) 541-7823  
FAX: (919) 541-2860

Dwight Mowery  
Division of Extramural Activities  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 1004  
Bethesda, MD 20892  
Telephone: (301) 496-9231  
FAX: (301) 402-0219

#### AUTHORITY AND REGULATIONS

The programs of the NIA, NIAID, NIDCD, NIEHS, and NINDS are identified in the Catalog of Federal Domestic Assistance, Nos. 93.173, 93.866, 93.856, 93.113, and 93.854, respectively. Awards are made under authorization of the PHS Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

**5333 Westbard Avenue  
Bethesda, MD 20816**

# NIH GUIDE

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## For Grants and Contracts

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**National Institutes of Health Room B4BN23,**  
**Building 31, Bethesda, Maryland 20892**

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AND HUMAN SERVICES

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21, No. 43  
November 27, 1992

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National Institutes of Health

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FUNDING STRATEGIES FOR FY 1993

NIH GUIDE, Volume 21, Number 43, November 27, 1992

P.T. 34; K.W. 1014006

National Institutes of Health

These core principles will serve to guide Institutes and Centers (I/Cs) in their funding decisions on Research Project Grants (RPGs) in FY 1993. In general, these principles are similar to those developed for FY 1992.

Non-Competing RPGs

1. The award of non-competing grants at committed levels is the cornerstone of the NIH Financial Management Plan and is the basis of our credibility with the Congress and the scientific community.
2. Non-competing grants, on the average, cannot exceed 4 percent over the prior budget period, taking into account one-time, non-recurring costs such as equipment.
3. Every effort will be made to accommodate shifts in the NIH fiscal situation. If conditions are such that funding at the committed levels is not possible, the I/Cs will consult with the Deputy Director for Extramural Research, NIH, to determine an appropriate resolution.

Competing RPGs

1. The average total cost of the cohort of competing grants in one fiscal year will not increase by more than the Biomedical Research and Development Price Index (BRDPI), 5.08 percent in FY 1993, over the cohort of competing grants in the previous fiscal year (including Small Business Innovation Research grants). Given the appropriation level for FY 1993, some I/Cs may not be able to provide an increase consonant with the BRDPI.
2. In making funding decisions, I/Cs should factor in the total costs of a grant, especially at the margin.
3. Budgetary reductions will be achieved through a combination of initial review and Council/Board recommendations, program and staff review for cost allowability and reasonableness, and programmatic adjustments, where necessary, to arrive at an appropriate funding level.
4. Adjustments made on the basis of initial review or Council/Board recommendations, or determinations of the allowability/reasonableness of costs, as well as programmatic adjustments to arrive at an award level will be specifically documented. These may include adjustments of specific budget items, reductions in investigator effort, or decreases in the number of specific aims. The I/Cs plans, i.e., general rationale and methodology, for programmatic adjustments will be based on considerations at the program level.
5. Award reductions of 25 percent or more below the IRG recommended level on a single grant application may require a revised statement of specific aims and a revised budget from the principal investigator, properly countersigned by the institution, which must be reviewed and approved by program and grants management staff. Program staff, in consultation with the principal investigator and grants management staff, will decide if a new statement of specific aims is required.
6. For competing continuation grants, one factor in arriving at the award amount will be the level of support in prior years and the extent to which the I/C can permit growth within the existing constraints on increases in average costs.
7. The average length of research project grants will be four years (excluding Small Business Innovation Research grants).

INQUIRIES

For further information, contact the grants manager or Health Scientist Administrator responsible for your grant.

REMINDER AND UPDATE: REQUIREMENT FOR INSTRUCTION IN THE RESPONSIBLE CONDUCT OF RESEARCH IN NATIONAL RESEARCH SERVICE AWARD INSTITUTIONAL TRAINING GRANTS

NIH GUIDE, Volume 21, Number 43, November 27, 1992

P.T. 44; K.W. 1014004, 1014006

National Institutes of Health

Since July 1990, the National Institutes of Health (NIH) has required all applications for Institutional National Research Service Award (NRSA) Research Training Grants (T32, T34) to include a description of a program to provide instruction in the responsible conduct of research. This requirement was announced in the NIH Guide for Grants and Contracts on December 22, 1989 (Vol. 18, No. 45), and again on August 17, 1990 (Vol. 19, No. 30).

With this notice, the NIH updates and reinforces the commitment to ensure that all NRSA supported trainees are provided an opportunity for training in the responsible conduct of research. Plans for instruction in the responsible conduct of research will continue to be required in all applications for institutional NRSA research

training grants. But, beginning with applications for research training grants received on or after January 10, 1993, this requirement will be modified as follows:

- o Applications without plans for instruction in the responsible conduct of research will be considered incomplete and will be returned to the applicant without review.
- o Every predoctoral and postdoctoral NRSA trainee supported by a T32 or T34 institutional research training grant must receive instruction in the responsible conduct of research.
- o Plans that incorporate instruction in the responsible conduct of research for all graduate students and postdoctorates in a training program or department, regardless of the source of support, are particularly encouraged.
- o Although the NIH will not establish specific curriculum or format requirements, all programs are strongly encouraged to consider instruction in the following areas: conflict of interest, responsible authorship, policies for handling misconduct, policies regarding the use of human and animal subjects, and data management.
- o Plans must address: the subject matter of the instruction, the format of the instruction, the degree of faculty participation, trainee attendance, and the frequency of instruction. A rationale for the proposed plan of instruction must be provided.
- o Progress reports on the type of instruction provided, topics covered, and other relevant information such as attendance by trainees and faculty participation must be included in future competing and noncompeting applications.

The procedures for the review of the plans for instruction in the responsible conduct of research will be as follows:

- o At initial review, one or more reviewer(s) will be assigned to evaluate the plan for providing training in the responsible conduct of research.
- o The plan will be discussed after the overall determination of merit so that the quality of the plan will not be a factor in the determination of the priority score.
- o The assessment of the plan will include consideration of the appropriateness of the topics, the format, the amount and nature of faculty participation, and the frequency and duration of instruction. Plans will be judged either acceptable or unacceptable.
- o The plan and its acceptability will be described in an administrative note in the summary statement.
- o Regardless of the priority score, applications with unacceptable plans will not be funded until a revised, acceptable plan is provided by the applicant. The acceptability of the revised plan will be judged by staff within the awarding component at the NIH.

#### INQUIRIES

The contact for general information about this policy is:

Dr. Walter T. Schaffer  
Director, Research Training and Special Programs Office  
National Institutes of Health  
Building 31, Room 5B44  
Bethesda, MD 20892  
Telephone: (301) 496-9743

Questions regarding a specific training program or grant application should be directed to the appropriate NIH Institute.

#### THE ETHICS OF CLINICAL RESEARCH ON HUMAN SUBJECTS: FACING THE 21st CENTURY

NIH GUIDE, Volume 21, Number 42, November 20, 1992

P.T. 42; K.W. 0783005

National Institutes of Health

The National Institutes of Health (NIH) Office for Protection from Research Risks (OPRR) is co-sponsoring with the University of Texas Medical Branch, Galveston a conference to discuss the ethical issues associated with clinical research involving human subjects. This conference is open to anyone with an interest in research involving human subjects and may be of special significance for individuals serving on Institutional Review Boards.

DATES: February 28 through March 2, 1993

LOCATION: San Luis Hotel  
5222 Seawall Boulevard  
Galveston, TX 77551  
Telephone: 1-800-392-5937

SPONSORS: The University of Texas Medical Branch at Galveston Galveston, Texas, National Institutes of Health, Office for Protection from Research Risks, Bethesda, MD

REGISTRATION AND INFORMATION: Ms. Sharon Goodwin  
Institute for the Medical Humanities  
301 University Boulevard, M-11  
The University of Texas Medical Branch  
Galveston, TX 77555-1311  
Telephone: (409) 772-2376

This national/international conference will explore the ethics of clinical research on human subjects. The goals of this timely meeting include:

- (1) providing a forward-looking analysis of the major ethical issues now facing biomedical researchers and institutions;
- (2) critically examining research ethics as set forth in the Belmont Report and other position papers of the two National Commissions;
- (3) enabling researchers and research-oriented administrators to plan effectively for future research initiatives; and
- (4) providing a forum for discussion and collaboration between IRB members and ethicists.

#### INQUIRIES

Ms. Roberta Sonneborn  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-7163

#### NATIONAL HUMAN SUBJECT PROTECTIONS WORKSHOPS

NIH GUIDE, Volume 21, Number 42, November 20, 1992

P.T. 42; K.W. 0783005

National Institutes of Health  
Food and Drug Administration

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in research. The workshops are open to everyone with an interest in research involving human subjects. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. Issues discussed at these workshops are relevant to all other Public Health Service agencies. The current schedule includes the following:

#### SOUTHEASTERN WORKSHOP

DATES: January 14 and 15, 1993

LOCATION:  
Sheraton Sand Key Resort  
1160 Gulf Boulevard  
Clearwater Beach, FL 33515  
Telephone: (813) 595-1611

SPONSORS:  
University of South Florida  
Florida A & M University

REGISTRATION:  
Ms. Eileen Highsmith  
Executive Secretary  
University of South Florida  
4202 E. Fowler Avenue (MP.FAO-126)  
Tampa, FL 33620-7900  
Telephone: (813) 974-2897

TITLE: Barriers to Informed Consent: Language, Age Factors, Trauma, and Women/Minority Issues

DESCRIPTION: Today's researchers face numerous barriers to obtaining an informed consent. Such issues as age, language, mental capacity, and sobriety may affect the ability of subjects to give a truly informed consent. Many of these barriers oftentimes impact the pool of subjects which an investigator is willing (or able) to use in a research project. In addition, recent legislation from the Congress was designed to address the issue of inadequate numbers of women and minorities in research projects. This conference has been designed to address three main areas in which barriers to informed consent may exist: mental competence, ethnic and gender issues, and research with children and the elderly.



The conference program is designed to be of value to physicians, nurses, pharmacists, scientific investigators, and other health care professionals. All IRB members, students in health care areas and administrators will also benefit from the conference. Attention will be given to Federal regulations governing research on human subjects, with special emphasis placed on the assessment of risks---medical, legal, and psychosocial. Ample opportunities will be provided to exchange ideas and interests, through question and answer sessions and informal discussions.

#### **SOUTHWESTERN WORKSHOP**

**DATES:** February 12 and 13, 1993

**LOCATION:** Sheraton Tempe Mission Palms Hotel  
60 East 5th Street  
Tempe, AZ 85281  
Telephone: (602) 894-1400

**SPONSORS:** Arizona State University  
Northern Arizona University

**REGISTRATION:** Ms. Carol Jablonski  
IRB Coordinator  
Office of the Assistant Vice President for Research  
Arizona State University  
Tempe, AZ 85287-3403  
Telephone: (602) 965-6788

**TITLE:** Contemporary Issues in Human Subject Research: Challenges for Today's IRBs

**DESCRIPTION:** This program is designed to be a practical working session to explore contemporary issues in human subjects protection including regulations and assurances, categorization of research protocols, uses of special populations, experimental design and scientific merit, fetal tissue research, ethical/legal issues in human subjects research, and conflict of interest. As appropriate, topics will be discussed from the perspective of the clinical researcher and the behavioral/social science researcher. Issues will be discussed in a panel format with ample time for audience questions. An outstanding faculty has been assembled.

This program should be of interest to researchers in clinical medicine and the behavioral and social sciences. Institutional Review Board members, university and hospital administrators, lawyers, ethicists, health care practitioners, students, and other persons with interests in human subject protection issues.

#### **SOUTHWESTERN WORKSHOP**

**DATES:** February 28 through March 2, 1993

**LOCATION:** San Luis Hotel  
5222 Seawall Boulevard  
Galveston, TX 77551  
Telephone: (800) 392-5937

**SPONSORS:** The University of Texas Medical Branch at Galveston

**REGISTRATION:** E. Ray Stinson, Ph.D.  
Office of Sponsored Programs-Academic  
The University of Texas Medical Branch at Galveston  
Galveston, TX 77555-1311  
Telephone: (409)-772-3482

**TITLE:** The Ethics of Clinical Research on Human Subjects: Facing the 21st Century

For further information regarding these workshop and future NIH/FDA National Human Subject Protections Workshops, please contact:

Ms. Darlene Marie Ross  
Division of Human Subject Protections  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-8101

#### **WORKSHOP ON MINIMIZING PAIN AND DISTRESS IN LABORATORY ANIMALS**

**NIH GUIDE,** Volume 21, Number 42, November 20, 1992

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health (NIH), Office for Protection from Research Risks (OPRR), is continuing to sponsor workshops on implementing the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Each of the workshops scheduled for FY 1993 will focus on a specific theme.

NIH Guide for Grants and Contracts - Vol. 21, No. 43 - November 27, 1992

The workshops are open to institutional administrators, members of Institutional Animal Care and Use Committees, laboratory animal veterinarians, investigators and other institutional staff who have responsibility for high-quality management of sound institutional animal care and use programs.

Opportunities will be available through workshops, question periods, and informal discussions for participants to exchange ideas and interests with faculty and OPRR representatives.

DATE: December 3-4, 1992

TOPIC: Minimizing Pain and Distress in Laboratory Animals

LOCATION: Loews Vanderbilt Plaza  
2100 West End Avenue  
Nashville, TN 37203  
Telephone: (615) 320-1700  
FAX: (615) 320-5019

SPONSORS: Vanderbilt University  
Meharry Medical College

REGISTRATION: Ms. Marilyn Dasaro  
Division of Continuing Medical Education  
Vanderbilt University  
D-8211 Medical Center North  
Nashville, TN 37232-2337  
Telephone: (615) 322-4030  
FAX: (615) 343-0809

DATE: January 21-22, 1993

LOCATION: Sheraton Grande Torrey Pines  
10950 N. Torrey Pines Road  
La Jolla, CA 92037  
Telephone: (619) 558-1500  
FAX: (619) 558-1131

SPONSORS: Scripps Clinic and Research Foundation  
Salk Institute

REGISTRATION: Janie Partridge  
Scripps Clinic and Research Foundation/MB  
10666 North Torrey Pines Road  
La Jolla, CA 92037-000  
Telephone: (619) 554-8048  
FAX: (619) 554-8841

TOPIC: Science and Animals: Addressing Contemporary Issues

DESCRIPTION: The Workshop will include the topics, Institutional Responsibility and Current Issues of Concern; Biohazard Concerns in Animal Research, e.g., HIV in scid-hu Chimeric Mice, Herpes B in Nonhuman Primates, SIV in Nonhuman Primates; Animal Care and Use Concerns in Neuroscience Research; IACUC Responsibility and special concerns.

The Workshop is designed for Institutional Animal Care and Use Committee (IACUC) members, institutional administrators, laboratory animal veterinarians, investigators and their staff, as well as any person sharing responsibility for the management of a sound institutional animal care and use program.

For information concerning content and logistics at the program, please contact Janie Partridge at (619) 554-8048, FAX (619) 554-8841.

DATE: June 10-11, 1992

TOPIC: TO BE ANNOUNCED

LOCATION: Oklahoma City Marriott  
3233 Northwest Expressway  
Oklahoma City, OK 73112  
Telephone: (405) 842-6633  
FAX: (405) 842-3152

SPONSOR: University of Oklahoma Health Sciences Center

REGISTRATION: Ms. Marilyn Perry, Assistant to Director for Compliance  
Division of Animal Resources  
BMSB/Room 203  
University of Oklahoma Health Sciences Center  
Telephone: (405) 271-5185  
FAX: (405) 271-3032

## INQUIRIES

For further information concerning future NIH/OPRR National Animal Welfare Education programs contact:

Ms. Roberta Sonneborn  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31, Room 5B59  
Bethesda, MD 20892  
Telephone: (301) 496-7163

## NOTICES OF AVAILABILITY (RFPs AND RFAs)

### PREPARATION OF RADIOLABELED SPHINGOLIPIDS

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFP AVAILABLE: NIH-NINDS-93-03

P.T. 34; K.W. 1003006, 1003012

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS), NIH, has a requirement for the preparation and delivery of certain synthesized radiolabeled sphingolipids needed to support basic and clinical investigations of Gaucher's disease, Niemann-Pick disease, and Fabry's disease conducted by staff of the Division of Intramural Research, NINDS.

The Contractor shall be required to prepare and deliver: (a) a total of 3.0 grams of 14-C-glucocerebroside (1.0 gram during the basic contract period, and 1.0 gram during each option period) specifically labeled in the D-glucose portion of the molecule with a minimum specific activity of 1000 d.p.m. per nanomole; (b) 1.0 gram of 14-C-sphingomyelin (to be delivered during the first option period) labeled in the choline portion of the molecule with a minimum specific activity of 1000 d.p.m. per nanomole; and (c) 1.0 gram of 14-C-ceramidetrihexoside (to be delivered during the second option period) labeled exclusively in the terminal molecule of galactose with a minimum specific activity of 1000 d.p.m. per nanomole. The labeled sphingolipids shall be synthesized with radiochemical purity and in the form of the naturally occurring stereoisomers. The homogeneity of each sphingolipid delivered shall be documented by elemental analysis, various physical methods including infrared, NMR, and mass spectroscopy, thin-layer or high-pressure liquid chromatography. The specific radioactivity of the various compounds shall be certified.

Offerors will be required to provide evidence of their competence, ability, and prior experience in the synthesis of radioactive sphingolipids.

This requirement represents a recompetition of work currently being performed under NINDS Contract No. N01-NS-0-2386, with Lipitek, Inc. It is expected that the incumbent Contractor will recompet.

One award is anticipated. Award will be made on a fixed-price per deliverable basis. The basic contract will cover a 12-month term and will contain two fixed-price, one year options.

This is not a Request for Proposals (RFP). RFP No. NIH-NINDS-93-03 will be issued on or about December 1, 1992, with January 29, 1993, set as a tentative closing date for receipt of proposals.

To receive a copy of the RFP, submit a written request to the following address, and supply two self-addressed mailing labels:

Contracts Management Branch, DEA  
National Institute of Neurological Disorders and Stroke  
Federal Building, Room 901  
7550 Wisconsin Avenue  
Bethesda, MD 20892

Reference: RFP No. NIH-NINDS-93-03

This announcement does not commit the NINDS to make an award. All responsible sources may submit a proposal that will be considered by the agency.

### CAPABILITY FOR THE CONSTRUCTION OF RECOMBINANT MALARIA VACCINES

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFP AVAILABLE: NIH-NIAID-DMID-93-11

P.T. 34; K.W. 0740075, 0760060, 0760080, 0755010

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) has a requirement for a malaria vaccine design. This requirement is for a facility and team of scientists to synthesize, using recombinant DNA technology, and to express biological constructs encoding polypeptide products based on malaria antigens. This

requirement is part of a cooperative initiative with the Agency for International Development. Respondents must have facilities and equipment to allow the construction of recombinant antigen genes from known sequences and cloned DNA specimens, the efficient expression of polypeptide products of such recombinant gene constructs, and protein purification. Quality control, including assessment of protein purity and immunologic evaluation of synthesized polypeptide products in animal models, must also be a part of the capability. The government will work closely with the contractor in the selection and design of the candidate genes and expression systems. The contractor will also participate and assist in development of Investigational New Drugs (IND) applications. Scaled-up production according to current Good Manufacturing Practices, clinical trials, and aspects of the preclinical evaluation of the polypeptide products of the recombinant genetic constructs, will be conducted at other facilities.

Any contract awarded will be subject to DHHS regulations regarding the animal subjects in research. One contract may be awarded as a result of this solicitation. It is expected that the contract will have a three-year period of performance. The issuance of the Requests for Proposals (RFP) will be on or about November 23, 1992 and proposals will be due by the close of business on January 15, 1993. Any responsible offeror may submit a proposal that will be considered by the Government.

#### INQUIRIES

To receive a copy of the RFP, provide this office with two self-addressed mailing labels. Requests for the RFP may be directed to:

Merilee Rahe-Stoline  
Contract Specialist, Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
6003 Executive Boulevard, Room 3C07  
Bethesda, MD 20892

This advertisement does not commit the Government to award a contract.

#### STORAGE, REPACKAGING AND DISTRIBUTION OF INVESTIGATIONAL AGENTS FOR AIDS

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFP AVAILABLE: NIH-NIAID-DAIDS-93-14

P.T. 34; K.W. 0715008, 0780000

National Institute of Allergy and Infectious Diseases

The Pharmaceutical and Regulatory Affairs Branch (PRAB) of the Treatment Research Operations Program (TROP), Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID) is seeking a contractor to operate and maintain a Clinical Research Products Management Center for investigational agents used in clinical trials sponsored by the DAIDS. This center receives shipments from a variety of sources, stores the study products under specified conditions, provides inventory and distribution record maintenance, and ships to clinical study sites. In some cases, packaging and/or labeling, including patient specific packaging, is required. A computerized data processing system will be used for record keeping and other functions. The contractor must possess distributor's, manufacturing and Drug Enforcement Agency (DEA) licenses as well as an Environmental Protection Agency (EPA) toxic waste generator permit. This is an announcement for an anticipated Request for Proposal (RFP). RFP NIH-NIAID-DAIDS-93-14 will be issued on or about November 30, 1992 with a closing date tentatively set for January 14, 1993.

#### INQUIRIES

To receive a copy of the RFP, supply this office with three self-addressed mailing labels. Requests for the RFP are to be directed in writing to:

Brenda J. Velez, Contracting Officer  
6003 Executive Boulevard  
Solar Building, Room 3C07  
National Institute of Allergy and Infectious Diseases  
Bethesda, MD 20892  
Telephone: (301) 496-7117

Telephone inquiries will not be honored and all inquiries must be in writing. A short version of the RFP will be provided first, which includes only the Work Statement and the Evaluation Criteria to be used for selection of the awardee. After examining this, a full text version of the RFP must be requested in writing for those offerors interested in responding. FAX requests are acceptable for the full text version only (FAX 301-402-0972). All proposals from responsible sources will be considered by the NIAID. This advertisement does not commit the Government to make an award. No collect calls will be accepted.



# CLINICAL COORDINATING CENTER FOR THE ANGIOGRAPHIC TRIAL IN WOMEN

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFP AVAILABLE: NHLBI-HV-92-42

P.T. 34, II; K.W. 0755018, 0755015, 1004008, 0715040

National Heart, Lung, and Blood Institute

The primary objective of this project is to assess whether or not interventions that modify lipoproteins will inhibit progression and induce regression of coronary plaques in women; the secondary objective is to elucidate the mechanisms by which various treatments may modify atherosclerosis in women. The study will consist of three randomized angiographic trials with a common core protocol and a single Clinical Coordinating Center. Angiographic changes will be primary endpoints of all three trials. A total of 568 women with angiographically documented coronary artery disease will be enrolled to participate in one of three randomized therapeutic trials: (1) Hormone replacement therapy in postmenopausal women; (2) Cholesterol-lowering diet and antioxidants; and (3) Drugs that lower LDL-cholesterol versus drugs that, in addition, raise HDL-cholesterol levels. The program will comprise three phases. During Phase I, the Clinical Coordinating Center will participate with investigators from three to six Clinical Centers to develop detailed protocols and Manuals of Operations and to assume the responsibility for a cooperative effort with other study investigators to develop, pretest, reproduce, and distribute appropriate reporting forms. The Clinical Coordinating Center will also be responsible for establishing and working with a central laboratory facility, a central angiographic facility for quantitative coronary angiography, and a drug distribution center. The Clinical Coordinating Center will design quality control and randomization procedures. During Phase II, the Clinical Coordinating Center will be responsible for randomizing patients, monitoring recruitment, and collecting, editing, storing, and analyzing data. Throughout the course of the study, the Clinical Coordinating Center will assume the responsibility for review of the quality and timeliness of the data transmitted. The Clinical Coordinating Center will prepare reports for the Data and Safety Monitoring Board that will monitor progress of the program. During Phase III, the Clinical Coordinating Center will analyze the data and prepare and write scientific reports and manuscripts for publication and presentation, in collaboration with other study investigators and the National Heart, Lung, and Blood Institute's Program Office. One award is anticipated. This incrementally funded contract will be awarded for five years.

This announcement is not a Request for Proposals (RFP). RFP NHLBI-HV-92-42 will be released on or about November 25, 1992 with proposals due on or about February 1, 1993. One award is anticipated by the Government. The written request must include three self-addressed mailing labels, and must cite RFP No. NHLBI-HV-92-42.

## INQUIRIES

Request for copies of the RFP are to be sent to:

Sharon M. Kraft, Contract Specialist  
HLVD Contracts Section, COB, DEA  
National Heart, Lung, and Blood Institute  
Bethesda, MD 20892  
Telephone: (301) 496-6815

# CLINICAL CENTERS FOR THE ANGIOGRAPHIC TRIAL IN WOMEN

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFP AVAILABLE: NHLBI-HV-92-43

P.T. 34, II; K.W. 0755015, 0715040, 0706030, 0760025

National Heart, Lung, and Blood Institute

The primary objective of this project is to assess whether or not interventions that modify lipoproteins will inhibit progression and induce regression of coronary plaques in women; the secondary objective is to elucidate the mechanisms by which various treatments may modify atherosclerosis in women. The study will consist of three randomized angiographic trials with a common core protocol and a single Clinical Coordinating Center. Angiographic changes will be primary endpoints of all three trials. A total of 568 women with angiographically documented coronary artery disease will be enrolled to participate in one of three randomized therapeutic trials: (1) Hormone replacement therapy in postmenopausal women; (2) Cholesterol-lowering diet and antioxidants; and (3) Drugs that lower LDL-cholesterol versus drugs that, in addition, raise HDL-cholesterol levels. Angiographic changes will be primary endpoints of all three trials. Quantitative computerized analysis of the angiograms will be performed by a central angiographic facility. In addition, it is proposed to follow lipid and clotting parameters, which will be analyzed by a central laboratory facility. The study population for the first and third trials will consist of 208 women, and the second, 152 women, with angiographically documented CAD defined as at least 30 percent but no more than 75 percent occlusion of any single coronary artery. The following will be exclusion criteria: (1) age over 75; (2) any condition that would compromise participation in the study or the likelihood of obtaining exit angiograms, such as a life-threatening disease or a chronic illness likely to require frequent hospitalizations and/or treatment adjustments that may affect outcome variables; (3) contraindications to the use of any of the study interventions; and (4) clear need for treatment with any of the interventions for this trial. It is estimated that 50 percent of eligible women requiring angiographic evaluation will agree to participate in the study, and 50 percent of these women will meet the angiographic criteria. Three to six awards are anticipated. These incrementally funded contracts will be awarded for five years.

This announcement is not a request for proposals (RFP). RFP NHLBI-HV-92-43 will be released on or about November 25, 1992 with proposals due on or about February 1, 1993. Written request must include three self-addressed mailing labels and must cite RFP No. NHLBI-HV-92-43.

#### INQUIRIES

Request for copies of the RFP are to be sent to:

Sharon M. Kraft, Contract Specialist  
HLVD Contracts Section, COB, DEA  
National Heart, Lung, and Blood Institute  
Bethesda, MD 20892  
Telephone: (301) 496-6815

#### DATA COORDINATION CENTER FOR COOPERATIVE COMMUNITY-BASED PERINATAL STUDIES AND INTERVENTIONS IN MINORITY POPULATIONS

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFA AVAILABLE: HD/NR/OMP-93-010

P.T. 34, FF; K.W. 0755018, 0770005, 0775025, 0403004

National Institute of Child Health and Human Development  
National Center for Nursing Research  
Office of Minority Programs

Letter of Intent Receipt Date: January 15, 1993  
Application Receipt Date: February 18, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute of Child Health and Human Development (NICHD), in cooperation with the National Center for Nursing Research (NCNR) and the Office of Minority Programs (OMP), invites applications for a cooperative agreement to participate as the Data Coordination Center (DCC) in support of planning and conducting research to address the problem of the unacceptably high infant mortality rate among minority populations in this country. Specifically, the Institutes will assist the community (using a cooperative agreement mechanism) in establishing a model population based perinatal epidemiology and clinical research effort to conduct research that is aimed at increasing the understanding of the determinants of the high infant mortality rate in Washington, DC, and developing and testing interventions intended to reduce infant mortality and its related outcomes, such as low birth weight, intrauterine growth retardation, and preterm delivery.

A Data Coordination Center for the network of research organizations established via a prior RFA (HD/NR/OMP-92-07) will provide management support and consultation in the design, execution, and analysis for multi-institutional observational and experimental studies in the field of infant mortality, and will ensure that the studies are of the highest scientific integrity and meet rigorous statistical standards. The Data Coordination Center will be functionally independent of all research sites, although it could be physically located at one of them.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Data Coordination Center for Cooperative Community-Based Perinatal Studies and Interventions in Minority Populations, is related to the priority areas of infant mortality, fetal deaths, low birth weight, high risk pregnancies, and prenatal care. It is a component of the Infant Mortality Initiative of the PHS and the Minority Health Initiative of the National Institutes of Health (NIH). Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by for-profit and non-profit organizations, public and private, within easy commuting distance of the District of Columbia. Institutions may submit singly or in partnerships with two or more organizations or groups.

#### MECHANISM OF SUPPORT

The funding mechanism to be used to assist the community in undertaking this coordinated population-based research effort, including behavioral interventions and clinical trials, will be the research demonstration cooperative agreement (U18). This cooperative agreement provides support for testing, by means of a research design, the effectiveness of the transfer and application of techniques or interventions derived from a research base for the control of diseases or disorders, or for the promotion of health. The project should be capable of making conclusions which are generally applicable to other sites.

The major difference between a cooperative agreement and a research project grant is that there will be substantial programmatic involvement of the NICHD Project Coordinator above and beyond the levels required for traditional program management of grants. (Grants Policy Statement, DHHS Publication (OASH) 90-50,000 (rev. 10/01/91)). Specifically, a member of the NICHD scientific staff will cooperate with Principal Investigators as a partner in the projects and serve as the Project Coordinator. All parties will agree to accept the participatory and cooperative nature of the group process. Since the OMP and the NCNR are cosponsoring this initiative, NCNR and OMP representatives will also participate as partners.

#### FUNDS AVAILABLE

The estimated funds available for support of the entire program for the first year of the initiative (covered by a prior RFA), which will consist primarily of planning and protocol development, are \$500,000 total costs. Supplemental funds will be added in future years to cover costs of the implementation and evaluation of protocols. Due to the reissuing of this RFA, no Data Coordination Center costs will be incurred for the first year of the initiative (FY 92). The FY 93 budget has appropriated up to \$5,000,000 total cost for this purpose (for both the DCC and the six sites) for FY 93 (year 02 of the initiative). It is estimated that Data Center costs could be up to \$345,000 for year 01 for this award (Years 02/03 of the initiative). One award will be made for the Data Coordination Center. Although this program is provided for in the financial plans of the participating organizational entities, the award of a grant pursuant to this RFA is also contingent on the availability of funds for this purpose.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 09/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be checked. The signed, typewritten original of the application, including the checklist, and three exact photocopies must be sent to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, two additional copies of the application must be sent to:

Acting Director  
Division of Scientific Review  
National Institute of Child Health and Human Development  
6100 Building, Room 520 5E03A  
6100 Executive Boulevard  
Bethesda, MD 20892

Applications must be received by February 18, 1993. If an application is received after that date, it will be returned to the applicant without review. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the latter is withdrawn by the applicant. Nor will the DRG accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of such an application, but it must include an introduction addressing the previous critique.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It also allows staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to Dr. Heinz W. Berendes at the address listed under INQUIRIES.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged, and the opportunity to clarify any issues or questions from potential applicants is welcome.

Inquiries regarding programmatic issues and requests for the RFA may be directed to:

Heinz W. Berendes, M.D., M.H.S.  
Director, Division of Epidemiology, Statistics, and Prevention Research  
National Institute of Child Health and Human Development  
6100 Executive Boulevard, Room 7805  
Bethesda, MD 20892  
Telephone: (301) 496-5064



Inquiries regarding fiscal matters may be made to:

Mr. E. Douglas Shawver  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
6100 Executive Boulevard, Room 8A17F  
Bethesda, MD 20892  
Telephone: (301) 496-1303  
FAX: (301) 402-0915

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.865, Research for Mothers and Children. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC241), and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to review under the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SPECIALIZED CENTER OF RESEARCH IN SYSTEMIC LUPUS ERYTHEMATOSUS

NIH GUIDE, Volume 21, Number 43, November 27, 1992

RFA AVAILABLE: AR-93-02

P.T. 04; K.W. 0715015, 0710030, 0745027, 0745070

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: March 1, 1993

Application Receipt Date: April 20, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA AND GUIDELINES FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites applications for Specialized Centers of Research (SCORs) in Systemic Lupus Erythematosus. A SCOR is envisioned as a national resource, associated with a major medical complex and dedicated furthering the research effort related to systemic lupus erythematosus. A SCOR should foster a concerted research effort that strongly emphasizes basic disciplines, but also involves significant interaction between basic research and clinical investigations of systemic lupus erythematosus.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Specialized Center of Research in Systemic Lupus Erythematosus, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government that have established clinical programs in rheumatology and research programs in systemic lupus erythematosus. Foreign organizations are ineligible. International collaborations in domestic applications will only be accepted if the resources are clearly shown to be unavailable in the United States. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) specialized center grant (P50). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should be five years. The anticipated award date is September 30, 1993. The direct costs requested cannot exceed \$500,000 each year. Future SCOR awards or renewals will be by RFA only.

#### FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for new SCORs is \$1.5 million. Two awards are anticipated. However, funding will be contingent on receiving applications judged by peer review to be highly meritorious.



## RESEARCH OBJECTIVES

A SCOR provides a multidisciplinary approach and utilizes both laboratory and clinical research by providing for a mutually supportive interaction between basic scientists and clinical investigators. Research programs may vary at each institution according to local expertise, interests, and resources.

The objective of this SCOR program is to focus research on "bench to bedside" applications for the disease systemic lupus erythematosus. The research proposed should expedite development and application of new knowledge of specific importance to systemic lupus erythematosus and foster improved approaches to treatment and/or preventions. Emphasis in the proposed projects should be on the elaboration of new and significant hypotheses, development of innovative approaches, and generation of improved strategies for approaching current issues relating to systemic lupus erythematosus.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by March 1, 1993, a letter of intent that includes a descriptive title of the proposed research projects, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAMS staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Julia B. Freeman  
Centers Program, Extramural Programs  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 402-3348  
FAX: (301) 480-7881

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Special guidelines have been developed for the SCOR program in the NIAMS. These guidelines must be used in assembling the application. The guidelines may be obtained by contacting the Centers Program Director listed above.

Applications must be received by April 20, 1993. The RFA label available in the PHS 398 (rev. 9/91) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by the DRG and responsiveness by the NIAMS. Incomplete applications will be returned to the applicant without further consideration.

Applications may be triaged by an NIAMS peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications.

Additional scientific/technical merit criteria specific to the objectives of the SCOR program include:

- o scientific merit of combining the component parts into a SCOR;
- o technical merit and justification of each core unit;
- o adequacy of plans for interaction among investigators, and the integration of the various projects and core units;

o qualifications, experience and commitment of the SCOR Director and his/her ability to devote time and effort to provide effective leadership;

o scientific and administrative structure, including internal and external procedures for monitoring and evaluating the proposed research and for providing ongoing quality control and scientific review.

#### AWARD CRITERIA

Award decisions will be based on scientific merit of the applications. The anticipated date of award is September 30, 1993.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. Julia B. Freeman  
Centers Program, Extramural Programs  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 402-3348  
FAX: (301) 480-7881

Direct inquiries regarding fiscal matters to:

Mara H. DeKemper  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 732  
Bethesda, MD 20892  
Telephone: (301) 496-0552

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ONGOING PROGRAM ANNOUNCEMENTS

##### SMALL GRANT PROGRAM FOR THE NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

NIH GUIDE, Volume 21, Number 43, November 27, 1992

PAR: PAR-93-25

P.T. 34; K.W. 0715050, 0715055, 0705070, 041001

National Institute on Deafness and Other Communication Disorders

#### PURPOSE

This announcement supersedes all previously issued announcements for the National Institute on Deafness and Other Communication Disorders (NIDCD) Small Grant Program. This current Small Grant Program provides support for pilot research that is likely to lead to a subsequent Individual Research Project (R01) grant or a First Independent Research Support and Transition (FIRST) (R29) research project application. The research must be focused on areas within the mission of the NIDCD, that is, hearing, balance/vestibular, smell, taste, voice, speech, or language.

#### ELIGIBILITY REQUIREMENTS

Foreign organizations and institutions are not eligible. Current and previous recipients of NIH research grants such as small grant awards, R01, or R29 grants are ineligible for the Small Grant program. Individuals who have received research support from other Federal funding agencies are considered ineligible.

Participation in the program by investigators at minority institutions is encouraged.

Small grant funds may not be used to support thesis or dissertation research.

#### RESEARCH OBJECTIVES

The Small Grant program is designed solely to support basic and clinical scientists with limited research experience who are at the beginning stages of their research careers.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific questions(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

### APPLICATION PROCEDURES

Only one Small Grant application may be submitted by a Principal Investigator per receipt date. Applicants may not submit R01 or R29 applications on the same topic concurrently (to be considered at the same Advisory Council) with the submission of a Small Grant application.

The submission, review, and award schedule for the Small Grant Program is:

Receipt Dates for 1993	Institute Committee Review	Council Review	Earliest Funding
Jan 8	Feb-Mar	May	Jul
May 5	Jun	Oct	Dec
Sep 17	Oct-Nov	Jan	Apr

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

On the face page of the application: Item 2a Type "Small Grant Program NIDCD". Check the "YES" box.

Sections 1-4: Do not exceed a total of five pages for the following sections: specific aims, background and significance, progress report/preliminary studies, and experimental design and methods. A half-page introduction is acceptable only for revised applications. Applications that exceed the page limitation or NIH requirements for type size and margins will be returned to the investigator. The five page limitation does not include Sections 5-9 (Human Subjects, Consortia, etc.)

Section 3. Appendix materials are not allowed.

Use the mailing label in the application kit to mail the original and four copies of the application to:

To ensure that the application is received in sufficient time for the review, send one copy of the application to:

Chief, Scientific Review Branch  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892

#### REVIEW PROCEDURES

A review committee of the NIDCD will evaluate each Small Grant application in accord with the usual NIH peer review procedures and criteria. Applications will be evaluated with respect to the following criteria:

- o significance and scientific merit of the proposed project;
- o level of innovation;
- o investigator's potential for carrying out the research, as demonstrated by publication record and/or previous research/clinical experience or training relative to the goals and methods of the proposed study;
- o adequacy of the investigator's time commitment to the project;
- o potential of the proposed studies to lead to more extensive research;
- o adequacy of the facilities, supporting personnel, and available equipment for carrying out the proposed studies; and,
- o justifications of budget requests.

All applications subsequently will be reviewed by the National Deafness and Other Communication Disorders Advisory Council.

#### AWARD CRITERIA

The award of grants is contingent on the (1) receipt of applications of high scientific merit; (2) responsiveness to this announcement, including the eligibility of investigators; (3) relevance to the mission of NIDCD; and (4) the availability of appropriated funds.

Applicants may request up to \$25,000 (direct costs) per year. The grant may not exceed two years and is not renewable. Investigators are expected to seek continuing support for research through a research project grant (R01) or FIRST (R29) award.

#### INQUIRIES

For additional information, investigators are encouraged to call (301-496-5061) or write to NIDCD staff responsible for grants in the investigator's particular area of scientific interest:

Dr. Amy Donahue (hearing)  
Dr. Lynn Huerta (hearing)  
Dr. Kenneth Gruber (hearing)  
Dr. Daniel Sklare (balance/vestibular)  
Dr. Jack Pearl (chemical senses)  
Dr. Rochelle Small (chemical senses)  
Dr. Beth Ansel (voice, speech)  
Dr. Judith Cooper (language)

For budgetary and fiscal questions, contact:

Sharon Hunt  
Grants Management Officer  
National Institute on Deafness and Other Communication Disorders  
Executive Plaza South, Room 400-B  
6120 Executive Boulevard  
Rockville, MD 20892  
Telephone: (301) 402-0909

#### AUTHORITY AND REGULATIONS

Awards will be made under the authority of the Public Health Service Act, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. The program is not subject to the intergovernmental review requirements of Executive Order 12372 or to Health Systems Agency review.



# FOGARTY INTERNATIONAL RESEARCH COLLABORATION AWARD PROGRAM

NIH GUIDE, Volume 21, Number 43, November 27, 1992

PAR: PAR-93-026

P.T. 34, 48; K.W. 0715035, 0710030

Fogarty International Center

Application Receipt Dates: October 1, February 1, June 1

## PURPOSE

The Fogarty International Center (FIC) provides small grants referred to as Fogarty International Research Collaboration Awards (FIRCAs) to U.S. grantee institutions to facilitate cooperation and collaboration between U.S. scientists and scientists in Central and Eastern Europe, Latin America, and the non-U.S. Caribbean. This announcement expands the FIRCA program to include cancer-related collaborative research with scientists located in Sub-Saharan Africa. This new effort is supported by the National Cancer Institute (NCI). FIRCAs provide funds to foreign collaborators, through the U.S. grantee institution, for equipment and supplies at their home institution, and for travel expenses for both the U.S. Principal Investigator and the foreign collaborator. These awards are intended to support the new and expanded research efforts of U.S. scientists who are Principal Investigators of currently funded National Institutes of Health (NIH) research project grants on the general scientific subject of the proposed collaboration.

## ELIGIBILITY REQUIREMENTS

U.S. scientists who are Principal Investigators of NIH research project grants (R series, P series, or U-01 series) that will be active and funded during the proposed grant award period (up to three years) are eligible. The small grants will be made for work conducted in cooperation with scientists only in countries located in the geographical regions commonly known as Central and Eastern Europe (including the former USSR and the Baltic Republics), Latin America, the non-U.S. Caribbean, and for cancer-related research, Sub-Saharan Africa. The foreign collaborator must hold a position at a public or private non-profit institution that will allow him or her adequate time and provide appropriate facilities to conduct the proposed research.

## MECHANISMS OF SUPPORT

The small grants (R03) will provide up to \$20,000 per year for up to three years in direct costs. Funds may be used for materials, supplies, and equipment for the foreign scientist's research laboratory and for travel expenses for the Principal Investigator and/or the foreign collaborator and their research associates, as justified by the scientific needs of the project. No salaries or stipends for any of the collaborators, students, or technical assistants will be offered under these awards. Applicants must request support to conduct research not already being supported by the U.S. investigator's research grant; however, the research proposal should be an extension of or related to the currently funded research project. The awards will be made to U.S. institutions, which will be responsible for the expenditures. The minimum small grant project period will be for one year; the maximum will be for three years. Indirect costs will be calculated on the basis of the off-site rates of the U.S. sponsoring institution. The award of this small grant is non-renewable, and the NIH awarding unit of the "parent" grant is under no obligation to continue support for the foreign research component as a component of a recompeting "parent" grant.

## RESEARCH OBJECTIVES

The main objective of this program is to facilitate collaborative research efforts between U.S. and foreign scientists that will expand and enhance the NIH-supported research program of the U.S. Principal Investigator, while at the same time benefiting the scientific interests of the collaborating foreign scientist. These small grants will provide funds to purchase supplies, materials, and small equipment items necessary to conduct the collaborative research in the foreign scientist's research laboratory at a non-profit public or private institution in the eligible countries. These awards will also provide travel support, as necessary to conduct the collaborative research effort, for the U.S. and/or the foreign collaborator(s). All biomedical and behavioral research topics supported by the NIH are eligible for inclusion under this program in Central and Eastern Europe, Latin America, and the non-U.S. Caribbean. Research collaboration with scientists in Sub-Saharan Africa is limited to cancer-related research only. The U.S. Principal Investigator must show evidence of ongoing NIH research support in areas related to the small grant application, and this support must be available during the entire proposed small grant award period. The application must demonstrate that the effort will enhance the scientific contributions of both the U.S. and foreign scientists and strengthen the contribution to the NIH-sponsored research effort.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research finding can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women of minorities in a study design is inadequate to answer the scientific questions(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATIONS PROCEDURES

Applications are to be submitted by the U.S. Principal Investigator on the standard grant application form PHS 398 (rev. 9/91), available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, room 449, Bethesda, MD 20892, telephone (301) 496-7441. The deadlines for receipt of applications are October 1, February 1, and June 1 of each year. Special instructions are necessary and are available from the address below. Credentials for the foreign collaborators must be included with the application and the collaborative arrangements described in a letter signed by both investigators. Applicants must list the active NIH research grant(s) that will be held during the proposed project period of this award. The foreign laboratory collaborating with the Principal Investigator of the small grant must be located in the countries of Central and Eastern Europe (including the former USSR and the Baltic Republics), Latin America, the non-U.S. Caribbean and for cancer-related research, Sub-Saharan Africa.

The title and number of the announcement must be typed on line 2a of the face page of the application. The complete original and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned for review to, and awards will be made by, the FIC, utilizing the customary NIH peer review process. Scientific and technical merit will be evaluated by a Fogarty International Center initial review group. Second level review will be provided by the Fogarty International Center Advisory Board.

#### AWARD CRITERIA

Initial award decisions will be announced within a month following each board meeting and will be based on the scientific merit of the applications and the availability of funds.

#### INQUIRIES

Direct inquiries regarding programmatic issues and requests for the guidelines to:

Dr. Mirilee Pearl  
International Research and Awards Branch  
Fogarty International Center  
Building 31, Room B2C21  
Bethesda, MD 20892  
Telephone: (301) 496-1653  
FAX: (301) 402-0779.

Direct inquiries regarding fiscal matters to:

Ms. Silvia Mandes  
Grants Management Officer  
Fogarty International Center  
Building 31, Room B2C21  
Bethesda, MD 20892  
Telephone: (301) 496-1653  
FAX: (301) 402-0779

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.934. Awards are made under authorization of the Public Health Service Act, Title III, Sections 301 and 307(b) as amended, 42 USC 242(e). This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

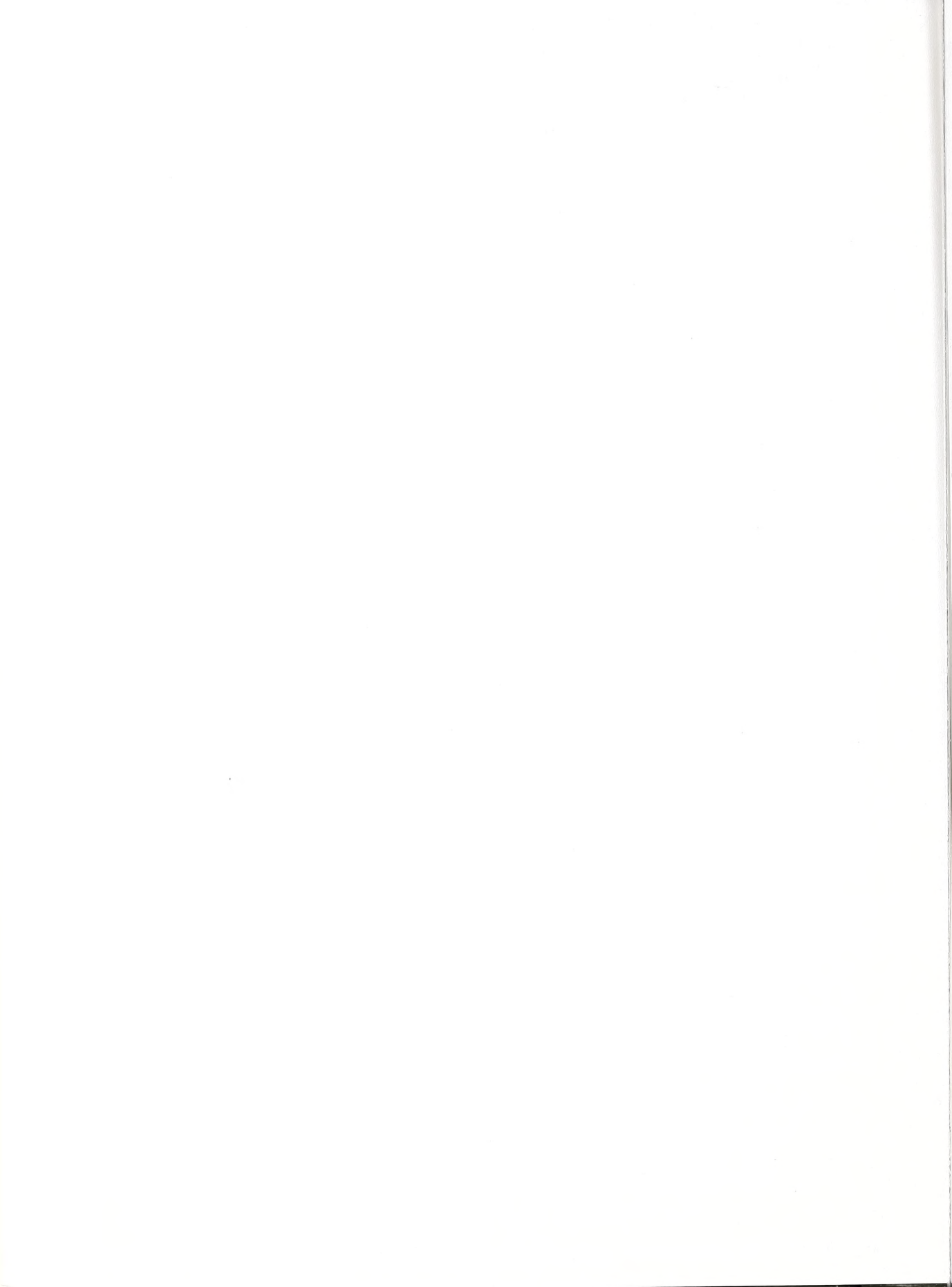
***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

5333 Westbard Avenue  
Bethesda, MD 20816

***THE NIH GUIDE TO GRANTS AND CONTRACTS WILL NOT BE PUBLISHED ON DECEMBER 4, 1992. THE NEXT ISSUE WILL BE ON DECEMBER 11, 1992.***

***HAPPY THANKSGIVING!!***











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# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

RICHARD W MURRY

\* 340189  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20879 0000

Vol. 21, No. 44, Part I of II  
December 11, 1992

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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*



## NOTICES

### WORLD AIDS FOUNDATION

NIH GUIDE, Volume 21, Number 44, December 11, 1992

P.T. 34, 42; K.W. 0715008, 0502017

Fogarty International Center

The World AIDS Foundation (WAF) announces its intent to support research and education relating to Acquired Immunodeficiency Syndrome (AIDS) in the developing world. The goal of the WAF is to facilitate information exchange and assist developing countries in responding to the AIDS pandemic.

The WAF is particularly interested in projects that are catalytic and once in place could have a multiplicative effect. The WAF also is particularly interested in supporting applications that originate from developing countries and that emphasize collaboration between and among scientists from developed and developing countries. The main area of interest of the WAF is education for health professionals in developing countries, especially in-country training. This includes highly focused workshops that enhance the scientific process and transfer knowledge needed in the effort against the Human Immunodeficiency Virus (HIV) infection and AIDS.

The limit of any single funding request to the WAF is \$200,000.

#### APPLICATION PROCEDURES

Concept letters and applications may be prepared in either English or French. Applicants should submit concept letters for initial consideration. Following review of concept letters, applicants may be invited to submit complete proposals. The annual deadline for receipt of concept letters is February 1.

#### INQUIRIES

Concept letters and inquiries concerning the programs of the World AIDS Foundation are to be directed by mail or by FAX to:

World AIDS Foundation  
Assistant Secretary for Health  
c/o Director, Fogarty International Center  
National Institutes of Health  
Building 31, Room B2C02  
Bethesda, MD 20892, U.S.A.  
FAX: (301) 402-2056

or

Fondation Mondiale SIDA  
c/o Directeur de l'Institut Pasteur  
28 rue du Docteur Roux  
75724 Paris, Cedex 15, FRANCE  
FAX: 0033-1-45688938

### NATIONAL CANCER INSTITUTE BRIEFING ON "THERAPEUTIC STUDIES OF PRIMARY CENTRAL NERVOUS SYSTEM MALIGNANCIES IN ADULTS"

NIH GUIDE, Volume 21, Number 44, December 11, 1992

P.T. 34; K.W. 0715035, 0705055, 0740015, 0740020

National Cancer Institute

Request for Applications (RFA) CA-93-03, for cooperative agreements (U01) from consortia of institutions to perform Phase I and II clinical evaluations of promising new chemotherapeutic or biologic agents for the treatment of primary central nervous system (CNS) malignancies was published in the NIH Guide for Grants and Contracts, Vol. 21, No. 41, November 13, 1992.

The National Cancer Institute (NCI) will hold a briefing session concerning this RFA on Tuesday, January 19, 1993 in Conference Room H, Executive Plaza North, 6130 Executive Boulevard, Rockville, MD to discuss this initiative and answer questions. Two sessions will be held from 9:00 a.m. to 11:00 a.m. and 2:00 p.m. to 4:00 p.m. Potential applicants may attend either session. All interested parties are invited to attend.

#### INQUIRIES

For further information and to register for the meeting, contact:

Ms. Diane Bronzert  
Cancer Therapy Evaluations Program  
Division of Cancer Treatment  
National Cancer Institute  
Executive Plaza North, Room 734  
Bethesda, MD 20892  
Telephone: (301) 496-8866  
FAX: (301) 480-4663

PREAPPLICATION CONFERENCE FOR WOMEN'S INTERAGENCY HEALTH STUDY

NIH GUIDE, Volume 21, Number 44, December 11, 1992

P.T. 42, II; K.W. 0710030, 0785035

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) is sponsoring a one-day preapplication conference concerning the Request for Applications (RFA) AI-92-12, Women's Interagency Health Study (WIHS). The conference is open to anyone interested in applying for a cooperative agreement award in response to this RFA. Issues to be discussed include application procedures, program goals and objectives, and award criteria. Time will be allocated for questions and answers.

DATE: December 18, 1992

CONFERENCE SITE: Bethesda, MD

INQUIRIES

Briana Porte  
The Mayatech Corporation  
1300 Silver Spring, MD 20910  
Telephone: (301) 587-1600

MANAGEMENT AND OPERATION OF THE NCI FREDERICK CANCER RESEARCH AND DEVELOPMENT CENTER

NIH GUIDE, Volume 21, Number 44, December 11, 1992

P.T. 34; K.W. 0780000, 1002002, 0780018, 0710030

National Cancer Institute

The National Cancer Institute (NCI) is seeking sources to perform research, operation and technical support, animal production, computer services, and scientific library services at the NCI Frederick Cancer Research and Development Center (NCI-FCRDC), a government-owned, contractor-operated facility that is a designated Federally Funded Research and Development Center (FFRDC). The facility consists of approximately 100 buildings and structures on 69 acres in Frederick, Maryland. The NCI intends to recompete this requirement which is presently being performed under five separate contracts as follows: Research, Contract N01-CO-74101, Advanced BioScience Laboratories, Inc.; Operations and Technical Support, Contract N01-CO-74102, Program Resources, Inc.; Animal Production, Contract N01-CM-23911, Harlan Sprague Dawley, Inc.; Computer Services, Contract N01-CO-74103, Data Management Services, Inc.; Scientific Library Services, Contract N01-CO-23913, Data Management Services, Inc.

All contracts are anticipated to be cost type, either cost-plus-fixed-fee or cost-plus-award-fee. Offerors will have the option of submitting multiple or combinatorial proposals. Anticipated beginning date of new contracts is September 26, 1994. Further notice will be published, including RFP availability, on or about March 1993. Term of resulting contract(s) is anticipated to be 10 years. Current annual negotiated amount for the last year of each contract: Research, \$15,156,672; Operations and Technical Support, \$155,588,664; Animal Production, \$3,522,562; Computer Services, \$1,457,207; Scientific Library Services, \$985,476.

This announcement is intended to apprise all interested organizations of this future full and open competition opportunity.

INQUIRIES

If additional information is required, contact

John Baker, Contract Specialist  
Frederick Cancer Research and Development Center  
National Cancer Institute  
P.O. Box B, Building 427  
Frederick, MD 21702-1201  
Telephone: (301) 846-1112

No collect calls will be accepted.

NOTICES OF AVAILABILITY (RFPs AND RFAs)

OPERATION OF THE NATIONAL ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFP AVAILABLE: HRSA-240-BHRD-2(3)

P.T. 34; K.W. 0780025, 0710125

Health Resources and Services Administration

The Division of Organ Transplantation has a requirement for an organization to operate and maintain the National Organ Procurement Transplant Network (OPTN). This acquisition will require that the organization have expertise in organ procurement and a board of directors that includes representatives of organ procurement organizations,

transplant centers, voluntary health associations, and the general public to establish in one location or through regional centers a system to match organs and individuals included on the list, especially individuals whose immune system makes it difficult for them to receive organs.

It is anticipated that only one award will be made to a private non profit organization. It is expected that the contract will have a three-year period of performance. Any responsible offeror may submit a proposal that will be considered by the government. Request for Proposals (RFP) HRSA-240-BHRD-2(3) will be issued on or about November 17, 1992. Proposals will be due on February 15, 1993.

#### INQUIRIES

To receive a copy of the RFP, supply this office with a request in writing and two self-addressed mailing labels addressed to:

Ms. Ann Linkins, Contract Specialist  
Contract Procurement and Operations Branch  
Health Resources and Services Administration  
Parklawn Building, Room 13A-19  
5600 Fishers Lane  
Rockville, MD 20857

This advertisement does not commit the government to make an award.

#### SCIENTIFIC REGISTRY FOR ORGAN TRANSPLANTATION

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFP AVAILABLE: HRSA-240-BHRD-3(3)

P.T. 34; K.W. 0780030, 0780025

Health Resources and Services Administration

The Division of Organ Transplantation has a requirement for the acquisition of Scientific Registry for Organ Transplantation. This acquisition will require maintenance of a computerized registry on all kidney, heart, liver, heart-lung, and pancreas transplant recipients at the time of transplant and periodically after transplant.

It is anticipated that only one award will be made to a private non profit organization. It is expected that the contract will have a three-year period of performance. Any responsible offeror may submit a proposal that will be considered by the government. Request for Proposals (RFP) HRSA-240-BHRD-3(3) will be issued on or about November 17, 1992. Proposals will be due on February 15, 1993.

#### INQUIRIES

This advertisement does not commit the government to make an award. To receive a copy of the RFP, supply this office with a request in writing and two self-addressed mailing labels addressed to:

Ms. Ann Linkins, Contract Specialist  
Contract Procurement and Operations Branch  
Health Resources and Services Administration  
5600 Fishers Lane, Room 13A-19  
Rockville, MD 20857

#### RESEARCH LEADING TO IMPROVED MEASLES VACCINES

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: AI-93-06

P.T. 34; K.W. 0715125, 0740075

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 11, 1993  
Application Receipt Date: March 11, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

Measles recently reemerged as a public health problem in the U.S. and measles continues to be a deadly disease in the developing world. The purpose of this RFA is to acquire the information needed for the development of safe new measles vaccines that are highly efficacious when administered in early infancy and that will aid in the control and eventual eradication of measles. An expanded research effort is needed for the rational development and evaluation of new vaccines and immunization strategies. The National Institute of Allergy and Infectious Diseases (NIAID) requests investigator-initiated research grant applications focused on the study of measles virus and the host's response to infection as it relates to the safe induction of long-lasting protective immunity in individuals, and the reduction of measles disease and infant deaths in populations.

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Research Leading to Improved Measles Vaccine, is related to the priority area of immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) (R29) award. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01) and the FIRST (R29) award mechanisms (if interinstitutional collaborations are anticipated, contact Dr. James M. Meegan at the address listed under INQUIRIES). The total project period for applications submitted in response to the present RFA may not exceed five years. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will also vary. If the proposed budget exceeds \$200,000, the Principal Investigator must obtain a written waiver from Dr. James Meegan to submit with the grant application. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all unsolicited investigator-initiated applications and be reviewed according to the customary NIH peer review procedures.

#### FUNDS AVAILABLE

There are \$1.5 million available in total support (direct plus indirect costs) for this RFA for the first year. It is anticipated that six to eight new awards will be made, none to exceed \$200,000 in total annual direct costs.

#### RESEARCH OBJECTIVES

A major epidemic of measles occurred in 1989-90, and measles reemerged as a significant health problem in the U.S. The major cause of the reemergence of measles in the U.S. was the failure to vaccinate children at the appropriate age, rather than failure of vaccine efficacy. However, current vaccines do have some deficiencies as public health tools, particularly in regard to efficacy in very young infants. Infants are at greatest risk during the interval between loss of maternal antibody and receipt of vaccine. Thus, both internationally and domestically, there is an urgent need for an efficacious vaccine that can be safely administered at six to nine months of age or earlier in infancy. Furthermore, future programs aimed to increase immunization coverage will emphasize administration at earlier ages in infancy of current as well as new, multiple combinations of vaccines.

This announcement is intended to stimulate innovative research on measles across several research disciplines, with a strong emphasis on studies to develop improved vaccines that can safely overcome the maternal antibody barrier and induce long-lasting protective immunity. Research projects are sought that investigate topics including, but not limited to, those listed below.

- o Determination of which measles antigens are required to safely elicit long-lasting, protective humoral and cellular immunity in the developing immune system of the young infant.
- o Characterization of the quantitative and qualitative differences between vaccine-induced and naturally-induced protective immunity.
- o Elucidation of the impact of maternal antibody on infant immunization, and development of strategies to overcome maternal antibody as a block to immunization in very young infants.
- o Development of an animal model of measles virus infection and disease that parallels human disease and that could be used to study the many host and viral factors influencing establishment of protective immunity in the young infant.
- o Establishment of the viral correlates of virulence and attenuation.
- o Investigation of measles virus pathogenesis, including virus-induced immune suppression.
- o Elucidation of viral and host factors contributing to immunization-induced adverse events.
- o Pre-clinical development of highly efficient methods for the safe delivery of appropriate measles antigens leading to establishment of protective immunization.
- o Application of research on closely related viral systems, such as distemper, to address specific problems related to immunization of young infants.

#### SPECIAL REQUIREMENTS

Principal Investigators should budget for an annual one-day progress review meeting at the NIH.



## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

### LETTER OF INTENT

Prospective applicants are asked to submit, by January 11, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAID staff to estimate the potential review workload and to avoid possible conflict of interest in the review. The letter of intent is to be sent to Dr. James M. Meegan at the address listed under INQUIRIES.

### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-496-7441.

Applications must be received by the receipt date of this RFA. Applications not received by the receipt date will be considered nonresponsive to this RFA and the applicant will be contacted to determine whether to have the application returned to the applicant or be processed as an unsolicited application for the next DRG review cycle.

### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by the DRG and responsiveness by the NIAID. Incomplete applications will be returned to the applicant without further consideration. If the application is complete but not responsive to the RFA, it will undergo the same process as for late applications. Complete and responsive applications will be evaluated for scientific/technical merit by an appropriate scientific review group. The second level of review will be provided by the NIAID National Advisory Council.

Review criteria to be used are generally the same as those for unsolicited research grant applications.

### AWARD CRITERIA

The anticipated date of award is September 1993. Awards will be made solely on the basis of priority score, programmatic balance, and available funds.

### INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome.

Send the letter of intent, requests for the RFA, and inquiries regarding programmatic issues to:

Dr. James M. Meegan  
Virology Branch, Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3A15  
Bethesda, MD 20892  
Telephone: (301) 496-7453  
FAX: (301) 496-8030

Direct inquiries regarding fiscal matters to:

Mr. Todd C. Ball  
Grants Management Branch, Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B35  
Bethesda, MD 20892  
Telephone: (301) 496-7075

### Schedule

Letter of Intent Receipt Date:	January 11, 1993
Application Receipt Date:	March 11, 1993
Scientific Review Date:	July 1993
Council Meeting Date:	September 1993
Earliest Award Date:	September 1993

This program is described in the Catalog of Federal Domestic Assistance No. 93.856, Microbiology and Infectious Diseases Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**RADIOLOGIC DIAGNOSTIC ONCOLOGY GROUP V: STEREOTACTIC BREAST BIOPSY FOR NON-PALPABLE LESION CHARACTERIZATION**

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: CA-93-01

P.T. 34; K.W. 0715035, 0706030, 0745020

National Cancer Institute

Letter of Intent Receipt Date: January 12, 1993

Application Receipt Date: March 12, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

**PURPOSE**

The Radiation Research Program (RRP), Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI), invites applications for cooperative agreements to establish a multi-institutional scientific group in order to optimize a clinical algorithm for non-palpable breast lesion characterization.

**HEALTHY PEOPLE 2000**

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Radiologic Diagnostic Oncology Group (RDOG) V: Stereotactic Breast Biopsy for Non-Palpable Lesion Characterization, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0, or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

**ELIGIBILITY REQUIREMENTS**

Non-profit and for-profit organizations and institutions, governments and their agencies, and foreign and domestic institutions are eligible to apply. Applications from minority individuals and women are encouraged. Applications may be submitted from institutions that desire to be a participating clinical institution in a consortium and/or as a headquarters institution. The same institution may serve in both capacities within this cooperative agreement.

**MECHANISM OF SUPPORT**

Awards will be made as cooperative agreements (U01), a funding mechanism in which substantial NCI programmatic involvement with the recipients during performance of the planned activity is anticipated. Applicants will be responsible for the planning, direction, and execution of the proposed project.

**FUNDS AVAILABLE**

Approximately \$1,500,000 in total costs per year for four years will be committed to fund applications that are submitted in response to this RFA. It is anticipated that a consortium of about ten clinical institutions and the headquarters component will be funded to establish the RDOG V. It is anticipated that approximately one-fourth of the total funds expended each year will be devoted to the headquarters function, and approximately three-quarters will be awarded to the participating Clinical Institutions.

**RESEARCH OBJECTIVES**

The objective of this RFA is to invite applications to perform centrally coordinated multi-institutional cooperative clinical trials to develop an optimal clinical algorithm for characterization of small non-palpable breast cancers. The successful applicants will form RDOG V. The results of the RDOG V studies should have a direct and immediate impact on management of minimal breast cancer. Sufficient numbers of patients must be available in each institution for successful completion of the proposed clinical trials.

**Background**

The RDOG was formed by the NCI in September 1987. The RDOG objective is timely evaluation of current and emerging imaging modalities in the management of patients with cancer. The development of multi-institutional clinical trial groups allows for rapid patient accrual within a short period of time. This in turn ensures rapid evaluation and optimization of imaging techniques for diagnosis, staging, and serial monitoring of cancer.

The RDOG has had a significant impact on clinical research in radiology. This is the first time that multi-institutional clinical trials in diagnostic imaging have been conducted in a centrally coordinated fashion with strict quality control and analysis of cost-effectiveness. Ultimately, RDOG study findings would be useful for design of therapeutic protocols and formulating clinical and medical insurance reimbursement policy.

Since the time of its establishment, RDOG clinical research has been important for the development of optimal imaging algorithms for prostate and lung cancer (RDOG I), pancreatic and colon cancer (RDOG II) and musculoskeletal and head and neck tumors (RDOG III). In the near future, RDOG IV will be established to study pediatric solid tumors and ovarian cancer. This RFA will establish RDOG V in order to evaluate stereotactic breast biopsy as a minimally invasive, low morbidity alternative for open surgical biopsy.

#### SPECIAL REQUIREMENTS

The administrative and funding mechanism to be used to support these awards will be a cooperative agreement (U01) between each awardee and the NCI. In a cooperative agreement there is substantial Federal programmatic involvement above and beyond the levels characteristic of traditional program management of grants. Prospective applicants must obtain a copy of the RFA for additional information.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women and minorities are not included in the study populations, a specific and compelling justification for this exclusion must be provided. Applications that do not include women and minorities and that are without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 12, 1993, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, it is requested in order to provide an indication of the number and scope of applications to be reviewed.

The letter of intent is to be sent to Dr. Faina Shtern at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441; and from the NCI program director named below. Submit a signed, typewritten original of the application, including the Checklist, and three signed, exact photocopies, in one package to the address below. The photocopies must be clear and single sided.

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission, send two additional copies of the application to:

Referral Officer  
Division of Extramural Activities  
National Cancer Institute  
Room 838, Westwood Building  
Bethesda, MD 20892

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the DRG for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the program requirements and criteria stated in the RFA is an NCI program staff function. Applications that are judged non-responsive will be returned to the applicant by the NCI, but may be submitted as investigator-initiated research grants at the next receipt date. Questions concerning the responsiveness of proposed research to the RFA may be directed to program staff listed under INQUIRIES.

If the number of applications submitted is large compared to the number of awards to be made, the NCI may conduct a preliminary scientific peer review (triage) to eliminate those that are clearly not competitive. The NCI will remove from competition those applications judged to be noncompetitive for award and notify the applicant and institutional business official.

Those applications judged to be both competitive and responsive will be further evaluated according to the review criteria stated in the RFA for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review by the National Cancer Advisory Board considers the special needs of the NCI and the priorities of the National Cancer Program.

## INQUIRIES

Direct requests for the RFA and inquiries regarding programmatic issues to:

Faina Shtern, M.D.  
Chief, Diagnostic Imaging Research Branch  
Radiation Research Program  
National Cancer Institute  
Executive Plaza North, Suite 800  
Bethesda, MD 20892  
Telephone: (301) 496-9531

Direct inquiries regarding fiscal matters to:

Ms. Barbara Fisher  
Grants Management Coordinator  
Grants Administration Branch  
National Cancer Institute  
Executive Plaza South, Suite 242  
6120 Executive Boulevard  
Rockville, MD 20852  
Telephone: (301) 496-7800, Ext. 29  
FAX: (301) 496-8601

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.395, Cancer Treatment Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A. (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285), and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## HUMAN GENES FOR NON-INSULIN DEPENDENT DIABETES MELLITUS

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: DK-93-10

P.T. 34; K.W. 0715075, 0755035, 0755040, 0760015

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: February 18, 1993  
Application Receipt Date: March 17, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

## PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the American Diabetes Association (ADA) invites investigator-initiated research grant applications to identify specific genes responsible for non-insulin dependent diabetes mellitus (NIDDM) in humans. It is anticipated that this identification will require an interdisciplinary approach to develop and utilize strategies that will elucidate genes responsible for NIDDM using appropriate family pedigrees.

Applications will be submitted to the National Institutes of Health (NIH) and will be reviewed by NIH according to the usual NIH peer review procedures. Applications judged meritorious and designated for funding will be supported partially by the NIDDK and partially by the ADA through the issuance of coordinated but separate awards by the two funding organizations. Applicants are requested to provide the NIDDK with a letter of authorization to allow the NIDDK to provide a copy of their letter of intent, application, NIH-prepared summary statement of the initial review, and yearly progress reports, if funded, to the ADA. Applicants wishing to be considered for funding only by the NIDDK should so indicate in their letter of authorization. Under these latter circumstances, no information pertaining to their applications will be shared with the ADA.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Human Genes for Non-Insulin Dependent Diabetes Mellitus, is related to the priority area of diabetes and chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications for research grants may be made by public and private, foreign and domestic, for-profit and non-profit organizations, such as universities, colleges, hospitals and laboratories, units or State and local governments, and authorized units of the Federal government. Women and minority investigators are encouraged to apply.



## MECHANISM OF SUPPORT

This RFA will use the NIH research project grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years. The anticipated award date is September 30, 1993.

For the purpose of cost-containment, requested direct costs must not exceed \$160,000 per year for any single application. Applications exceeding this limit will not be reviewed as part of the RFA.

## FUNDS AVAILABLE

The NIDDK will commit up to \$2 million for first-year expenses, and additional funds for approved expenses in subsequent years for up to five years to fund applications submitted in response to this RFA. The ADA anticipates support of up to 20 percent of recommended direct costs for each funded application per year. The NIDDK and the ADA plan to make approximately 10 to 12 awards in FY 1993 contingent on the receipt of highly meritorious applications in response to this solicitation. With respect to post-award administration, the current policies and requirements that govern the research grant programs of the NIH will prevail for awards made by the NIDDK. Applicants should note that funds from the ADA will be subject to the indirect cost policy and post-award administration policies of the ADA. The award of grants pursuant to this RFA is contingent on the availability of funds for this purpose.

## SPECIAL REQUIREMENTS

### Letter of Authorization

Each applicant must submit a brief letter to the NIDDK indicating whether or not they wish their application to be considered for coordinated funding by the ADA. Although applicants may request that their applications be considered only by the NIDDK and not by the ADA, it is necessary that the record indicate the applicant's consideration of this opportunity. For each applicant who wishes to have the ADA consider their application for coordinated funding, all materials relating to the application will be promptly forwarded to that organization by the NIDDK, and the summary statement for the application will be shared with the ADA at the time of their availability. The NIDDK will provide no information to the ADA, nor any other non-governmental agency, related to applications from any applicant who requests that the ADA not consider their application. Letters of authorization should be prepared by the Principal Investigator and co-signed by the official signing for the applicant organization. This letter must be submitted as a cover letter accompanying the application.

## RESEARCH OBJECTIVES

NIDDM affects approximately 13 million Americans. It is the predominant form of the disease and severely impacts upon U.S. minority populations. This clustering of prevalence among ethnic/racial groups along with twin and family studies and animal models points to the genetic nature of this disease. Several genetic markers have been described as being associated with a rare form of NIDDM called Maturity Onset Diabetes of the Young (MODY) that shows autosomal dominant inheritance. One of these genetic markers is the gene for glucokinase, a key enzyme of glucose homeostasis found in the insulin-secreting beta cell of the pancreas and in the liver. This is the first evidence that a gene involved in glucose metabolism could be implicated in the pathogenesis of NIDDM. A variety of other genes may be related to the long-term complications suffered by those with all forms of diabetes.

Through this solicitation, the NIDDK and the ADA intend to stimulate investigator-initiated research designed to develop and utilize new molecular genetic strategies to provide a better understanding of the major genes involved in NIDDM in humans. To achieve this objective, appropriate family pedigrees may need to be collected as a prerequisite for the identification or for the verification of specific gene involvement. Since a large number of families may need to be recruited, accumulation of these families must be included within the framework of the proposed research plan. Utilization of existing sources of genetic material is encouraged. For example, the ADA is developing a repository of data, DNA, and cell lines of family pedigrees with NIDDM.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Potential applicants are strongly encouraged to submit a letter of intent by February 18, 1993. The letter of intent is to include: (1) names of the Principal Investigator/program director and principal collaborators, (2) descriptive title of the potential application, (3) identification of the organization(s) involved, and (4) the number and title of the RFA in response to which the application may be submitted.

The letter of intent is to be sent to:

Chief, Review Branch  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
5333 Westbard Avenue  
Bethesda, MD 20892

## APPLICATION PROCEDURES

Applications are to be submitted on form PHS 398 (rev. 9/91), that is available from an applicant institution's office of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. Use the conventional format for research project grant applications. To identify the application as a response to this RFA check "yes" on item 2a of page one of the application and enter the title "Human Genes for NIDDM" and the RFA number DK-93-10. Applications must be received by March 17, 1993.

## REVIEW CONSIDERATIONS

Applications in response to this solicitation will be reviewed using the usual NIH peer review procedures. For further details, applicants are referred to the RFA document.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Joan T. Harmon, Ph.D.  
Executive Director, Diabetes Research Program  
Division of Diabetes, Endocrinology and Metabolic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 622  
Bethesda, MD 20892  
Telephone: (301) 496-7731

Direct inquiries regarding fiscal matters to:

Betty E. Bailey  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.847, Diabetes, Endocrinology and Metabolism Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## EXTRAMURAL RESEARCH FACILITIES CONSTRUCTION PROJECTS

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: OD-93-01

P.T. 02; K.W. 0715035, 0715040, 0715032, 0715165, 0404009, 1002046

National Institutes of Health

Letter of Intent Receipt Date: February 17, 1993  
Application Receipt Date: March 30, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

## PURPOSE

Public Law Number 102-394, the Appropriations Act for the Department of Health and Human Services for Fiscal Year 1993, provides \$4,960,000 in the budget of the Office of the Director, National Institutes of Health (NIH) for extramural facilities construction grants, to be awarded competitively. The NIH announces the availability of an RFA, OD-93-01 for the construction of facilities of urgent national importance for biomedical/behavioral research and/or services to support such research. Applications for construction grants that were previously submitted to the NIH must recompile under this RFA.

The main objective of this construction program is to facilitate the conduct of biomedical/behavioral research by providing funds for construction of new facilities and for the purchase of associated fixed research equipment essential for the operation of these facilities. Support may be requested for the construction of new facilities and additions or renovations to existing facilities to meet the biomedical/behavioral research and/or services to support such research needs of an institution, or of a research group at that institution or elsewhere that utilizes the resources of that institution. The purpose of the proposed facility must be within the scope of one of the statutes authorizing the awards. Those statutes authorize construction grants that would benefit the fields of cancer, vision, heart, lung and blood, AIDS research, and drug abuse, pharmacotherapeutic research.

## ELIGIBILITY REQUIREMENTS

Domestic, non-Federal, public and private non-profit institutions, organizations, and associations that conduct or support biomedical/behavioral research are eligible to apply. An institution may submit only one application in response to this announcement. For example, a medical school and a dental school of the same institution, even when separated geographically, may not submit separate applications.

## MECHANISM OF SUPPORT

The award mechanism will be the construction grant award (C06). Awards will be administered under Federal Regulation 45 CFR Part 74 - Administration of Grants, and for cancer construction projects, 42 CFR Part 52b will also apply. Up to 50 percent of the allowable costs of a project may be awarded, not to exceed \$2,000,000. Prior to grant award, the applicant must provide an assurance of required matching funds and that additional funds will be secured to meet any projected costs in excess of the award amount. Requests of less than \$500,000 will not be accepted. No indirect costs or continuation costs will be awarded.

## FUNDS AVAILABLE

This one-time solicitation based on the Fiscal Year 1993 appropriation provides \$4,960,000 for this initiative. It is anticipated that three to four awards will be made.

## LETTER OF INTENT

Prospective applicants are asked to submit by, February 17, 1993, a letter of intent. The letter, requested for planning purposes only, must identify the RFA number, the proposed Principal Investigator, and include a brief title of the type(s) of research/research support to be conducted in the new facility. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIH staff to estimate the potential workload to avoid conflict of interest in the review. The letter of intent is to be addressed to Mr. Kenneth Brow at the address listed under INQUIRIES.

## APPLICATION PROCEDURES

Applicants must use Standard Form 424, Application for Federal Assistance. Application forms and the complete RFA must be requested from the staff contact official listed under INQUIRIES.

## REVIEW CONSIDERATIONS

Applications that are complete and responsive will be reviewed for scientific and technical merit by appropriate special peer review group(s) that will be convened by the Division of Research Grants, NIH. The second level of peer review will be conducted by the National Advisory Board or Council appropriate for the statutory authority that is applicable to the application. Detailed criteria on which the applications will be evaluated are discussed in the RFA.

## INQUIRIES

For additional information, a copy of the RFA, and application Standard Form 424 materials, contact:

Mr. Kenneth Brow  
Chief, Research Facilities Branch  
Division of Cancer Biology, Diagnosis, and Centers  
National Cancer Institute  
Executive Plaza North, Room 300  
Bethesda, MD 20892  
Telephone: (301) 496-8534

The programmatic and fiscal contacts are listed in the RFA.

## AUTHORITY AND REGULATIONS

Grants for research facilities construction programs of the National Institutes of Health are subject to Executive Order 12372. Awards will be made under the construction grants authorities in the Public Health Service Act, Title IV, Sections 413(b)(6)(B), 421(b)(2)(B), 455, 464P(b)(3), and Title XXIII, Section 2351(a)(7)(B) and administered under PHS grants policies and Federal Regulations 45 CFR Part 74 and for cancer construction only, 42 CFR Part 52b. This program is described in the Catalog of Federal Domestic Assistance, Number 93.392, Cancer-Construction.



## EXPRESSION OF TUBERCULOSIS IN THE LUNG

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: HL-93-12L

P.T. 34; K.W. 0715165, 0715125, 1002004, 0710070, 1002027, 1002019

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: February 15, 1993

Application Receipt Date: April 13, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) invites grant applications for support of research on elucidating the factors that are involved in expression of tuberculosis (TB) in the lung. The primary objectives of this grant program are to encourage research on understanding the factors involved in disease expression following infection by *Mycobacterium tuberculosis* (Mtb) and to determine the mechanisms by which such factors exert their influence on the lung.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Expression of Tuberculosis in the Lung, is related to the priority areas of HIV infection, and immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) (R29) awards. Applications from minority individuals and women are encouraged.

### MECHANISM OF SUPPORT

This mechanism of support for this RFA will be the research project grant (R01) or the FIRST (R29) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed five years. Requested budgets for FIRST (R29) awards may not exceed those specified in the FIRST (R29) award guidelines. The anticipated award date is September 30, 1993. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

### FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for the entire program is \$1.5 million. The expected number of new awards is six to eight. The specific number to be funded will, however, depend on the merit and scope of the applications received and the availability of funds.

### RESEARCH OBJECTIVES

The Centers for Disease Control estimates that since 1984 nearly 39,000 excess cases of TB have accumulated in the United States. This recent increase in TB morbidity is attributable, in large part, to TB occurring in persons infected with the Human Immunodeficiency Virus (HIV).

General approaches are being actively pursued in basic tuberculosis research but there is little research that relates to host defenses in the human lung and little or no effort is directed at the molecular and cellular mechanisms of TB expression in the lung. Almost no new information has been obtained on the basic mechanisms of protective immunity and the immune factors that contribute to the natural history of Mtb infection. A number of innate factors (age, gender, ethnicity) and associated disease states are thought to influence susceptibility/resistance and severity of disease when the lung responds to infection with Mtb. There has been no recent progress on obtaining information about the mechanisms by which such factors exert their influence on susceptibility/resistance or severity of TB disease.

The overall objective of this initiative is to encourage basic research on disease expression in the lung resulting from infection with Mtb. Applications are invited for innovative multidisciplinary approaches to identify the factors involved in disease expression, to determine their relationship to other factors of disease, and to better understand how such factors exert their influence on pathogenesis. Applications submitted in response to this announcement should clearly define the rationale, background, and specific aims of the proposed studies, and should provide a succinct description of the methods and procedures to be used.



Among topics relevant to the objectives of this RFA is research on the basic mechanisms of protective immunity against Mtb in the lung, including local anatomic and immunologic factors that contribute to lung injury, damage, or fibrosis, with particular emphasis on the molecular basis for the generation of immunopathology. Another area of interest is acquired resistance to tuberculosis and the role of T-helper lymphocyte-macrophage interactions in the ability of activated macrophages to ingest and kill virulent Mtb organisms. Since T-helper cells are known to be adversely affected by HIV infection and since the pathogenesis of TB in HIV-infected patients has been observed to differ from the classic granulomatous processes seen in HIV-negative individuals, research directed at obtaining more detail about the mechanisms of TB pathogenesis and the factors affecting susceptibility/resistance and severity in the presence of HIV infection is of particular interest in response to this initiative.

Since little is known about the mechanisms of reactivation of tuberculosis in the lung, the development of animal models that simulate reactivation disease and studies in humans that provide insights into the basic mechanisms of reactivation disease expression would also be desirable approaches. Basic research that addresses genetically determined and acquired local and systemic factors that affect immunity and disease expression in the lung would also be considered responsive to this initiative, as would studies elucidating the relationship between TB complicated by bronchiectasis and/or silicosis, and fibrosis.

Studies in humans are encouraged where possible. Investigators are also encouraged to consider other approaches that meet the goals of this program in addition to those cited.

#### SPECIAL REQUIREMENTS

Applications that propose descriptive studies in humans only and do not contain studies directed at uncovering mechanisms of disease or supporting hypotheses related to mechanisms of disease will not be acceptable. This program will not support studies directed at development of animal models alone. Models must be applied to the study of disease mechanisms associated with expression of tuberculous disease in the lung and wherever possible, the testing of hypotheses in the animal model should carry over to human studies. Applications that focus on the molecular biology and molecular immunology of expression of tuberculosis in the lung are of particular interest.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women and minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by February 15, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the names of any other participating institutions or investigators, and the number and title of the RFA in response to which the application may be submitted. A letter of intent is not binding, will not enter into the review of any application subsequently submitted, and is not a requirement for application. Such letters are requested for the purpose of obtaining an indication of the number of applications to be received. The NHLBI will not provide a response to a letter of intent. The letter is to be received no later than February 15, 1993 and sent to:

Chief, Centers and Special Projects Review Section  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 553  
Bethesda, MD 20892  
Telephone: (301) 496-7351  
FAX: (301) 402-1660

#### APPLICATION PROCEDURES

Applications must be received by April 13, 1993

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by NIH staff for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NHLBI staff will contact the applicant to determine whether to return the application or submit it for review in competition with unsolicited applications at the next review cycle.

Applications judged to be responsive will be reviewed for scientific and technical merit by an initial review group, convened by the Division of Extramural Affairs, NHLBI, solely to review these applications. Review criteria for this RFA are generally the same as those for unsolicited research grant applications.

## INQUIRIES

Written and telephone inquiries regarding this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Hannah H. Peavy, M.D.  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 6A09  
Bethesda, MD 20892  
Telephone: (301) 496-7034  
FAX: (301) 496-0886

Direct inquiries regarding review matters to:

Chief, Centers and Special Projects Review Section  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 553  
Bethesda, MD 20892  
Telephone: (301) 496-7351  
FAX: (301) 402-1660

Direct inquiries regarding fiscal matters to:

Raymond L. Zimmerman  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A17  
Bethesda, MD 20892  
Telephone: (301) 496-4970  
FAX: (301) 402-1200

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.838. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or to review by a Health Systems Agency.

## JUVENILE RHEUMATIC DISEASES RESEARCH CENTER PLANNING GRANT

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: AR-93-01

P.T. 34; K.W. 0715170, 0715010, 0710030

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: March 1, 1993  
Application Receipt Date: April 20, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA AND GUIDELINES FROM THE CONTACT NAME IN INQUIRIES, BELOW.

## PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites applications for a planning grant for a juvenile arthritis and musculoskeletal diseases center.

The goal of the planning grant is to explore the potential for establishing a Juvenile Rheumatic Diseases Research Center (JRDRS). The JRDRS planning grant will support development of key multidisciplinary research areas needed to establish a JRDRS.

A JRDRS is envisioned to be a resource center for research in juvenile arthritis and musculoskeletal diseases. This center will be associated with a major medical complex or consortium and will work in furthering the research effort related to juvenile arthritis and musculoskeletal diseases.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Juvenile Rheumatic Diseases Research Center Planning Grant, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments and eligible agencies of the Federal government. An established clinical and research program in areas pertaining to juvenile arthritis and musculoskeletal diseases should be present.

## MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) planning grant (P20). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should be three years. The anticipated award date is September 30, 1993. The direct costs requested cannot exceed \$200,000 each year. The award will not be renewed, but may be converted to another funding mechanism.

## FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for the JRDC planning grant is \$300,000. One award is anticipated. Funding will depend on receiving applications judged highly meritorious by peer review.

## RESEARCH OBJECTIVES

Chronic rheumatic diseases represent an important entity among chronic conditions affecting children. Among the rheumatic diseases seen in juvenile populations are rheumatoid arthritis, chronic arthritis (systemic, polyarthritic, and pauciarticular), spondyloarthritis, systemic lupus erythematosus, dermatomyositis, scleroderma and other vasculopathies and connective tissues disorders. Many childhood rheumatic diseases have orthopaedic aspects. A research agenda for the genetic, infectious, and immunologic aspects of juvenile rheumatic diseases will benefit from a multidisciplinary approach. Because the research issues are complex for juvenile arthritis and musculoskeletal diseases, the NIAMS seeks to explore the potential for establishing a JRDC through a planning grant.

The planning grant for a JRDC will provide funds for an administrative and planning core and for pilot studies to develop and expand the research base. Appropriate research areas include basic, clinical, and epidemiologic research as well as educational and psychosocial research.

## SPECIAL REQUIREMENTS

Investigators will be asked to meet periodically with NIAMS staff in Bethesda to review progress and plans for future work. The planning center will work with the NIAMS to hold a workshop to review the research agenda for juvenile arthritis. Applicants should include in the budget plans, appropriate travel costs for these meetings.

## STUDY POPULATIONS

### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by March 1, 1993, a letter of intent that includes a descriptive title of the proposed research projects, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAMS staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. Julia B. Freeman at the address listed under INQUIRIES.

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Special guidelines have been developed for the JRDC planning grant. These guidelines must be used in writing and assembling the application. The guidelines may be obtained by contacting the Centers Program Director listed under INQUIRIES.

Applications must be received by April 20, 1993. The RFA label available in the application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by Division of Research Grants (DRG) and responsiveness by the NIAMS. Incomplete applications will be returned to the applicant without further consideration.

Applications may be triaged by an NIAMS peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications.

Additional scientific/technical merit criteria specific to the objectives of the JRDR program include:

- o qualifications, experience and commitment of the Director (Principal Investigator) and his/her ability to devote time and effort to provide effective leadership;
- o scientific and administrative structure, including internal and external procedures for monitoring and evaluating the proposed research and for providing ongoing quality control and scientific review;
- o adequacy of plans for interaction among investigators, and the integration of the various projects and core units; and
- o potential for developing a JRDR from the resources and projects described.

#### AWARD CRITERIA

The anticipated date of award is September 30, 1993.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Julia B. Freeman  
Centers Program, Extramural Programs  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 402-3348  
FAX: (301) 480-7881

Direct inquiries regarding fiscal matters to:

Mara H. DeKemper  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 732  
Bethesda, MD 20892  
Telephone: (301) 496-0552

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### SKIN DISEASES RESEARCH CORE CENTERS

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA AVAILABLE: AR-93-03

P.T. 04; K.W. 0715185, 1003002, 0710070, 0710030

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: May 10, 1993

Application Receipt Date: June 18, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites applications for research core centers in skin diseases. The Skin Diseases Research Centers (SDRCs) will provide the resources



for a number of established, currently funded investigators, often from different disciplines, to adopt a multidisciplinary approach to common research problems in skin diseases and to ensure greater productivity than from each of the separate projects.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Skin Diseases Research Core Centers, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. A strong clinical and research program in skin diseases should be present. Foreign organizations are not eligible. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) core research center grant (P30). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA should be five years. The direct costs requested cannot exceed \$400,000 each year. The anticipated award date is March 1, 1994.

#### FUNDS AVAILABLE

The NIAMS intends to fund two SDRCs in FY 1994, subject to the availability of resources and receipt of sufficiently meritorious applications. The estimated funds (total costs) available for the first year of support is \$1.0 million.

#### RESEARCH OBJECTIVES

Research in skin diseases is at a stage where broad advances can be effectively fostered by research core centers. Examples of these areas include, but are not limited to:

- o stratum corneum: biochemistry, structure, function
- o epidermis: differentiation, keratinization, cellular constituents
- o dermal-epidermal junction: structure, functions, diseases
- o skin as an immunological organ
- o autoimmune skin diseases
- o dermis: structural components, diseases

The choice of research problem upon which the SDRC would focus is made by the principal and collaborating currently funded investigators.

The SDRC (P30) is a mechanism for integrating, coordinating, and fostering the interdisciplinary cooperation of a group of established investigators conducting programs of active, high-quality research that relate to a common theme. The SDRC provides support for:

1. Core resources and facilities to be used by investigators of individually supported research projects in order to enhance and coordinate their activities. This support may include personnel, equipment, supplies, services, and facilities.
2. Limited funds for pilot and feasibility studies.
3. Program enrichment activities.

#### SPECIAL REQUIREMENTS

Specific guidelines have been developed for the SDRC application and program. These guidelines may be obtained from the contact person listed under INQUIRIES.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by May 10, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows the NIAMS staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Julia B. Freeman  
Centers Program, EP  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 402-3348  
FAX: (301) 480-7881

#### APPLICATION PROCEDURES

Special guidelines have been developed for the SDRC program in NIAMS. These guidelines must be used in assembling the application. These guidelines may be obtained by contacting the Centers Program Director listed above.

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Applications must be received by June 18, 1993. The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page of the application.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by the DRG and responsiveness by NIAMS. Incomplete applications will be returned to the applicant without further consideration.

Applications may be triaged by an NIAMS peer review group on the basis of relative competitiveness. The NIAMS will withdraw from further competition those applications judged to be noncompetitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will undergo further scientific merit review. This review will be for scientific/technical merit by an appropriate peer review group convened by the NIAMS. The second level of review will be provided by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council.

#### AWARD CRITERIA

The primary factors determining the award will be the priority score and the availability of funds. Since the NIAMS is interested in funding only the best research, individual research projects of lesser quality may not be funded, even if approved, under the "umbrella" of the SDRC mechanism.

#### INQUIRIES

Written and telephone requests for the RFA and the opportunity to clarify any issues or questions from potential applicants are welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Dr. Julia B. Freeman  
Centers Program, EP  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 402-3348  
FAX: (301) 480-7881

Direct inquiries regarding fiscal matters to:

Mary L. Graham  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 722A  
Bethesda, MD 20892  
Telephone: (301) 402-3361

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

RFA AVAILABLE: HL-93-07-H

P.T. 34; K.W. 0706030, 0705015

National Heart, Lung, and Blood Institute (NHLBI)

Letter of Intent Receipt Date: July 5, 1993

Application Receipt Date: October 13, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

This solicitation will support grants for research and development of monoenergetic (10-20 eV) x-ray sources that can be hospital based and are clinically applicable for imaging cardiovascular structures. It is desirable that the proposed imaging system be tuneable with spectral concentration in a narrow band and at an intensity appropriate for specific cardiovascular imaging applications. A principal objective is to achieve improved image quality at lower radiation dose as compared with conventional x-ray imaging systems.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Monoenergetic X-ray Systems for Cardiovascular Imaging is related to the priority area of cardiovascular imaging. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-002-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Federal agencies must ensure that their own authorizing legislation will allow them to respond to this solicitation and to receive a PHS grant. Applications from minorities and women are encouraged.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years. This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to customary peer review procedures. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also.

#### FUNDS AVAILABLE

Approximately \$1.5 million in total costs will be provided for the first year of support for the entire program. It is anticipated that three to four new grants will be awarded under this program. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the National Heart, Lung, and Blood Institute (NHLBI), awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Administrative adjustments in project period and/or amount of support may be required at the time of the award.

#### RESEARCH OBJECTIVES

The proposed RFA seeks to support grant applications to study, develop, and evaluate minimally invasive x-ray systems using monoenergetic radiation to achieve improved resolution and image quality. Complete systems would need to be described, including both source and detector. Grant applications should propose a specific application, such as coronary artery imaging without intraarterial injection of contrast material, and include quantitative objectives for resolution, patient dose, and image quality. Grant applications should also emphasize close collaboration among physicists, biophysicists, radiologists, cardiologists, and bioengineers with both a theoretical basis and an experimental plan for the proposed system.

Grant applications may propose research in imaging systems for cardiovascular application utilizing monoenergetic or nearly monoenergetic x-ray sources and detector systems, including, but not limited to, the following technologies:

- o Transition x-ray sources
- o Channeling radiation sources
- o Cerenkov radiation sources
- o Smith-Purcell radiation sources
- o Parametric conversion systems
- o Coherent superlattice radiation systems
- o Free electron Laser systems

Each application must provide evidence that the proposed system is feasible as a hospital based facility, with size and cost estimates based upon calculations and experimental data.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by July 5, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of this RFA.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NHLBI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Chief, Centers and Special Projects Section  
Review Branch  
Division of Extramural Affairs  
National Heart, Lung and Blood Institute  
Westwood Building, Room 553A  
Bethesda, MD 20892  
Telephone: (301) 496-7351  
FAX: (301) 402-1660

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

Send or deliver a signed, typewritten original of the application, including the checklist, and three signed photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Send two additional copies of the application to the Chief, Centers and Special Projects Section, at the address listed under LETTERS OF INTENT.

Applications must be received by October 13, 1993.

#### REVIEW CONSIDERATIONS

Those applications that are complete and responsive will be evaluated for scientific/technical merit by an appropriate peer review group convened by the NHLBI. The second level of review will be provided by the National Heart, Lung, and Blood Advisory Council.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications. Although multidisciplinary approaches are encouraged, it is not the intent of this announcement to solicit applications for large studies that encompass a variety of independent projects, i.e., program projects.

#### AWARD CRITERIA

The most important criterion in selecting awardees will be the scientific merit. However, factors such as program balance and available funds may enter into selection from among competing applications.

The anticipated date of award is April 1, 1994

#### INQUIRIES

Inquiries regarding programmatic issues and requests for the RFA document be directed to:

Dr. Alan Berson or Dr. Rosalie Dunn  
Devices and Technology Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung and Blood Institute  
Federal Building, Room 312  
Bethesda, MD 20892  
Telephone: (301) 496-1586



Direct inquiries regarding fiscal and administrative matters to:

Mr. William Darby  
Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung and Blood Institute  
Westwood Building, Room 4A11  
Bethesda, MD 20892  
Telephone: (301) 496-7536

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grants policies and Federal Regulations, most specifically 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or to Health Systems Agency review.

***\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:***

***5333 Westbard Avenue  
Bethesda, MD 20816***



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# NIH GUIDE

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RICHARD W MURRY

\* 340109  
\*\*S1350E\*\*

929 WILD FOREST DRIVE  
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Vol. 21, No. 44, Part II of II  
December 11, 1992

ONGOING PROGRAM ANNOUNCEMENTS

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ONGOING PROGRAM ANNOUNCEMENTS

PSYCHOTHERAPY, BEHAVIOR THERAPY, AND COUNSELING IN DRUG DEPENDENCE TREATMENT

NIH GUIDE, Volume 21, Number 44, December 11, 1992

PA NUMBER: PA-93-27

P.T. 34; K.W. 0745060, 0404009, 0414014

National Institute on Drug Abuse

PURPOSE

The purpose of this Program Announcement (PA) is to encourage the study of psychotherapy, behavior therapy, drug abuse counseling, and other psychosocial interventions in the treatment of drug abuse and dependence. Studies involving the use of controlled clinical trials or other scientifically established research methods are encouraged. A secondary aim is to encourage the development of instruments to measure the process and outcome of psychotherapy/counseling of drug addicts and instruments that may be useful in determining therapist and patient characteristics predictive of treatment outcome. This announcement is intended to encourage the investigation of the treatment of individuals who are dependent upon cocaine, opiates, and other types of drugs (including polydrug abusers). This announcement is not intended to support therapy development research.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of Healthy People 2000, a PHS-led national activity for setting priority areas. This PA, Psychotherapy, Behavior Therapy, and Counseling in Drug Dependence Treatment, is related to the priority area of alcohol and other drugs. Potential applicants may obtain a copy of Healthy People 2000 (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign applicants are not eligible for First Independent Research Support and Transition (FIRST) awards (R29).



Support mechanisms include: research projects (R01), small grants (R03), and FIRST awards (R29). Most investigator-initiated research is supported by regular research grants. Research grants are awarded to institutions on behalf of Principal Investigators who have designed and will direct a specific project or set of projects. Except for small grants (R03) and FIRST awards (R29), investigator(s) may apply for a renewal (competing continuation) of the project by submitting an application for further support, including a report of progress and including specific plans for future work. For details on a particular support mechanism or program, contact the program staff listed under INQUIRIES.

## RESEARCH OBJECTIVES

### Background

Some form of psychotherapy, behavior therapy, or drug abuse counseling occurs in virtually every type of drug abuse/dependence treatment. Even where effective pharmacological treatments exist, such as the use of methadone for opiate dependence, they are usually administered with appropriate psychosocial/behavioral interventions (Grabowski et al., 1984).

Numerous behavioral interventions have been studied in attempts to improve the efficacy of drug abuse treatment. Contingency management has been shown to have some efficacy in medically withdrawing patients from methadone (Higgins et al., 1986) for some methadone-maintained individuals, but not all (Stitzer et al., 1986; Iguchi et al., 1988; Stitzer et al., 1992). Where the methadone dose has been decreased as a consequence to drug positive urine specimens, treatment dropout has been exacerbated (Stitzer et al., 1986; Iguchi et al., 1988). While it has been suggested that the use of "negative incentives" increases dropout rate, the extent to which the observed increases in dropout rate are due to methadone dose reduction per se has not been established.

Operant behavioral interventions appear to be most effective when integrated into a complete treatment package, as in the Community Reinforcement Approach (Hunt & Azrin, 1973; Azrin, 1976). This approach, originally developed for alcoholics, has been modified for cocaine abusers and has shown promise (Higgins et al., 1991).

Behavioral interventions based upon principles of classical conditioning, such as cue exposure, are also believed to have promise. When used as an adjunct to a comprehensive outpatient cocaine treatment program, patients given repeated cue exposure (to induce "extinction" to cocaine-related cues) evidenced better retention in treatment and fewer cocaine-positive urine specimens than patients not receiving the cue exposure (Childress, et al., 1992).

Individual cognitive-behavioral and psychodynamic as well as family approaches have all been demonstrated to have some efficacy (Stanton et al., 1982; Woody et al., 1983, 1987; Rounsaville et al., 1983; Carroll et al., 1991), but none has been demonstrated consistently to be more effective than another. This is congruent with findings in the psychotherapy research field at large; that is, it has not been consistently demonstrated that one type of psychotherapy is more effective than another (Luborsky et al., 1975; Smith & Glass 1977; Lambert et al., 1986; Stiles et al., 1986).

For particular subgroups of patients, however, there is reason to believe that particular types of therapies may be more useful than others. For example, there is some evidence that a structured, behavioral therapy may be more effective for substance abusers with sociopathic characteristics than an interactionally focused therapy (Kadden et al., 1989). In subgroups of patients with antisocial personality disorder who have an additional diagnosis of depression, cognitive-behavioral and supportive-expressive psychotherapy appears to be of some benefit. However, antisocial personality disorder alone appears to be a negative indicator for response to psychotherapy (Woody et al., 1985). There is also some evidence that the addition of psychotherapy to drug abuse counseling may be necessary for other subgroups of addicts. For example, in a methadone-maintenance program, drug abuse counseling is a sufficient complement to the treatment of opiate addicts with low levels of psychiatric severity. Providing psychotherapy to low psychiatric severity methadone-maintained opiate addicts who are already receiving drug abuse counseling does not appear to yield any further benefit (Woody et al., 1984). However, in methadone-maintained opiate addicts with high levels of psychiatric severity, psychotherapy in addition to drug abuse counseling is significantly more effective than drug counseling alone (Woody et al., 1984).

Inherent in doing research on psychosocial treatments for drug dependence are substantial methodological difficulties. Attrition is a problem in any form of behavioral treatment research, but especially so in drug dependence treatment. While there are numerous statistical procedures for dealing with the problem of attrition (Howard et al., 1990), none can replace lost data. It is, therefore, important to be aware of the ramifications of utilizing the array of available statistical techniques that are sometimes used to partially "correct" for lost data. Defining and including control groups as opposed to comparison groups (Borkovec, 1990) also presents a dilemma in comparative psychosocial treatment research. While there is no "perfect" design in such research, there are more or less perfect designs depending upon the research question we are asking. Other methodological and statistical issues, such as those dealing with therapist/counselor variance (Crits-Christoph et al., 1990) and choosing appropriate outcome measures (Lambert, 1990) are also important considerations and have been discussed at length elsewhere (Onken and Blaine, 1990).

Additional research is needed to answer a number of questions in this field such as:

1. Are certain strategies of drug abuse counseling/psychotherapy more effective than others in helping individuals achieve treatment goals?
2. In what way are various immediate treatment goals related to long-term outcome goals?
3. What is the relative efficacy of drug abuse counseling versus psychotherapy, and when and with whom is drug abuse counseling sufficient?

3. What populations of drug addicts (e.g., the dually diagnosed, racial and ethnic minorities, women, adolescents, etc.) require what types of counseling or psychotherapy?

5. How is the process of psychotherapy or counseling related to outcome in drug dependence treatment?

6. What are the characteristics of successful therapists, patients, and therapist/patient pairs?

#### Specific Areas of Interest:

1. Development of Psychotherapy/Counseling Instruments and Research Methods. Psychotherapy research, particularly with drug addicts, is in an early stage of development. The development and the refinement of instruments and methods that measure the theoretical constructs in the fields of psychotherapy and counseling are needed. Without instruments that measure these constructs in a valid and reliable manner, the controlled, scientific study of psychotherapy and counseling is impossible.

Investigators are encouraged to develop new instruments and refine existing instruments from the mental health field that can be used in controlled psychotherapy/counseling research studies with drug addicts. The development of valid and reliable instruments that measure various aspects of the process and strategies of psychotherapy/counseling, the immediate goals and outcome of these treatments, therapist characteristics predictive of treatment outcome, and patient characteristics predictive of outcome are encouraged.

2. Comparative Psychosocial Treatment Research with Drug Addicts. Controlled clinical trials that examine the relative efficacy of psychotherapy, behavior therapy, counseling, pharmacotherapy, and the many combinations of these forms of treatment with various populations of drug addicts are encouraged. The goal of such comparative treatment research is not to determine which treatments "win," but, rather to determine which treatments are most efficacious with which populations, and under what conditions. Studies that investigate the relative efficacy of individual, group, or family psychotherapy, behavior therapy, and drug abuse counseling in patients with various co-morbid Axis I and Axis II disorders are particularly encouraged. Investigations that compare the efficacy of one form or combination of psychotherapy, behavior therapy, or counseling to another in other subpopulations of drug addicts (e.g., racial and ethnic minorities, pregnant women, and individuals who abuse cocaine intravenously) are also encouraged. Where effective pharmacotherapies are available, research projects that attempt to maximize the efficacy of that pharmacotherapy through integration with psychosocial treatment are encouraged.

Applicants proposing comparative psychosocial treatment research studies are encouraged to examine the interactions of relevant therapist/patient characteristics with therapy type and to assess the relative contribution of therapist, patient, and type of therapy to treatment outcome.

For these studies, it is imperative that investigators accurately measure and control for the psychiatric diagnosis and problem severity level of the patients. It is also necessary that clear definitions of treatment outcome variables be specified, and that valid and reliable measures of outcome be used. It is recommended that therapists/counselors providing the treatment be systematically trained, that manuals be used to guide the treatments, that valid and reliable therapist competence and adherence scales be used, and that the treatment process be measured accurately. For all efficacy studies, it is recommended that adequate followup assessments be planned. It is also important that these studies use procedures and methods that can be replicated. It is strongly suggested that pilot data showing that a counseling or psychotherapy strategy is promising be provided when proposing comparative research involving this treatment. These pilot data should indicate that the utilization of the therapy approach shows promise in its ability to produce a decrease in drug use, dropout rate, or psychiatric symptoms.

3. Research on Therapist and Patient Variables in Psychotherapy and Counseling. Researchers have highlighted the importance of individual differences among therapists and counselors independent of the form of treatment. Some studies have shown that certain therapists/counselors are more successful than others, and that this success is more related to the treatment provider than to the type of treatment provided (e.g., McLellan et al., 1988). Studies are sought that assess therapist and/or counselor characteristics and relate these characteristics to effective treatment. Studies that examine the interaction of therapist/counselor and patient variables as related to outcome are also encouraged. Additionally, studies that link the characteristics of patients with successful psychotherapeutic, behavioral, or drug abuse counseling treatment are desired. Measurements of therapist and patient characteristics should be obtained using psychometrically sound instruments. These studies should control for the type of treatment offered and should use objective, empirical measures of the treatment process that occurs.

4. Short-Term vs. Long-Term Goals of Drug Abuse Counseling/Psychotherapy/Behavior Therapy. The treatment process may be viewed as having two distinctive but interrelated sets of goals. One set involves long-term objectives to be achieved as a result of involvement in the treatment program. These goals include reduction in illicit drug use, reduction in illegal activities, improvement in social adjustment, etc. The other set of goals involves specific objectives to be achieved within the treatment program that, it is assumed, will allow clients to attain the long-term treatment goals. These immediate goals include assisting the client in recognizing the harm caused by drug dependence, developing personal strategies for reducing or avoiding stress, recognizing irrational ideas or beliefs, developing realistic strategies for interpreting life events, etc.

Research is needed to determine how immediate treatment goals are related to long-term treatment goals (i.e., how success in achieving goals within treatment is related to success in achieving goals that result from treatment). For example, investigators may wish to establish different measures of immediate treatment goals, evaluate clients on success in achieving those goals, and then relate success in attaining immediate treatment goals to outcome measures of drug use or social adjustment. Research is also needed to identify, operationally define, and compare the efficacy of different strategies for attaining immediate treatment goals. For example, investigators may wish to establish different measures of immediate treatment goals, evaluate clients on success in achieving those goals, and then relate success in attaining immediate treatment goals to outcome measures of drug use or social adjustment. Also, investigators may wish to establish two distinctive procedures for achieving stress management (or employment) by clients and then compare the efficacy of the two procedures in



terms of stress management. Controlled clinical trials or other rigorous research methods should be used.

5. **Component Analysis Research.** Knowing the effective components of treatment can greatly aid in improving the quality of treatment. Theoretically based research that attempts to determine the effective components or combination of components in drug dependence psychotherapies, behavior therapies, or counseling strategies is encouraged.

Where there is more than one way to answer a proposed research question, investigators are urged to state their theoretical, ethical, and practical reasons for choosing one research design over another (see Borkovec, 1990). Investigators should address the issues of selection bias and attrition (Howard et al., 1990), and any other pertinent methodological issues (see Onken and Blaine, 1990).

If a subject is identified as being at risk for HIV acquisition and/or transmission, HIV testing and counseling should be offered to the subject in accordance with current guidelines. Furthermore, in high-risk populations, investigators are encouraged to assess the effect of the new therapy on the acquisition/ transmission of associated infectious disease, including HIV.

#### STUDY POPULATION

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grant Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the application.

FIRST award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by an initial review group in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate national advisory council. Small grant applications (R03) do not receive a second-level review.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that Institute/Center/Division. The following will be considered in making funding decisions:

- o Scientific and technical merit of the proposed project as determined by peer review
- o Availability of funds
- o Institute program needs and balance

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applications is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Lisa Onken  
Treatment Research Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 10A-30  
Rockville, MD 20857  
Telephone: (301) 443-4060

Direct inquiries regarding fiscal matters to:

Mrs. Shirley Denney, Chief  
Grants Management Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.279. Awards are made under authorization of the Public Health Service Act, Section 301 and administered under PHS grants policies and Federal Regulations at Title 42 CFR Part 52, Grants for Research Projects, Title 45 CFR part 74 and 92, Administration of Grants, and 45 CFR Part 46, Protection of Human Subjects. Title 42 CFR Part 2, Confidentiality of Alcohol and Drug Abuse Patient Records, may also be applicable to these awards. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

Sections of the Code of Federal Regulations are available in booklet form from the U.S. Government Printing Office.

Awards must be administered in accordance with the PHS Grants Policy Statement, (rev. 10/90), which is available from institutional offices of sponsored research.

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NIH GUIDE, Volume 21, Number 44, December 11, 1992

PA NUMBER: PA-93-28

P.T. 34; K.W. 0404009, 0415001, 0404000

National Institute on Drug Abuse

#### PURPOSE

The purpose of this announcement is to encourage research to investigate entry, retention, and compliance in drug abuse treatment, and research on strategies to improve entry and retention in treatment, and to bring about compliance with program expectations and effectiveness of drug abuse treatment. An important focus of these studies will be on the various environmental and intrapersonal factors that promote drug abuse treatment entry, retention, compliance, and effectiveness. Research may be conducted in conjunction with clinical trials, evaluation studies, or through separate epidemiological and ethnographic studies.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of Healthy People 2000, a PHS-led national activity for setting priority areas. This Program Announcement (PA), Research to Improve Drug Abuse Treatment Entry, Retention, Compliance, and Effectiveness, is primarily related to the priority area of alcohol and other drugs. Potential applicants may obtain a copy of Healthy People 2000 (Full Report: Stock No. 017-001-00474-0, or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, non-profit and for-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply. Foreign applicants are not eligible for the First Independent Research Support and Transition (FIRST) awards (R29).

#### MECHANISM OF SUPPORT

Mechanisms available for support of this program include individual research applications (R01s), FIRST awards (R29s), and small grants (R03s). Small grants (R03s) and FIRST awards (R29s) may not apply for a renewal (competing continuation) of the project. For details on a particular support mechanism or program, contact the program staff listed under INQUIRIES.

#### RESEARCH OBJECTIVES

The treatment of drug abuse and addiction is a key part of the President's national drug control strategy. Two factors significantly affecting treatment outcomes are the length of time spent in treatment and the patient's during-treatment performance. Given the adverse health and other consequences of drug use and the scarcity of treatment resources, it is imperative that treatment effectiveness is improved by increasing patient retention and improving patient compliance with treatment.

The amount of time spent in treatment is one of the most significant predictors of favorable treatment outcomes. Research has shown that patients under legal sanction are likely to stay in treatment longer. Research has also addressed compliance with treatment expectations. Provision of enhanced services to treatment patients has also been shown to improve outcomes. Recent research has found that setting behavioral contingencies for take-home methadone privileges is an effective means of improving compliance with program expectations. As with other chronic diseases, there are compliance issues that interact with medication and behavior. Given high demand for drug abuse treatment relative to existing capacity and the need to improve drug abuse treatment outcomes, this announcement seeks to stimulate research projects that will increase knowledge about treatment compliance and retention.

#### Description of Program

Applications submitted under this announcement should focus on (1) research to understand factors and processes related to patient retention in treatment or compliance with program expectations; (2) research to test treatment innovations or strategies to enhance the ability of programs to retain patients or increase rates of program completion; and/or (3) strategies to improve patient compliance with program rules, expectations, and treatment goals. Studies under this announcement may involve analyses of existing data bases, collection of new data in programs, development and testing of identification and assessment methodologies to improve retention and compliance, or program-based studies of strategies for improvement in these areas. Investigation is encouraged in all treatment modalities (including methadone maintenance, medically supervised withdrawal from methadone with transition to counseling or self-help programs, drug-free outpatient, and therapeutic community or short-term residential/inpatient programs), although short-term treatment should be effectively linked to aftercare or continuing care arrangements. Compliance strategies that address aftercare are encouraged.

Studies of interventions may be comparative or controlled studies, but should utilize the best available and most appropriate research methodologies. Controlled studies should be based on well-defined patient groups entering treatment and treatment models that take into account identifiable stages of treatment at which program modifications are most likely to be needed in order to increase retention and compliance. Interventions can be pharmacological or nonpharmacological and may be based in a variety of settings (e.g., hospitals, residential programs, outpatient programs, correctional settings).

**Retention in treatment.** Although research has shown that successful outcomes are more likely if patients stay in treatment for 90 days or longer, early dropout rates in many drug abuse treatment programs are high. Research focused on studies of retention in treatment and strategies to improve retention, such as tailored interventions to reduce dropout in the critical induction period, is needed, as are studies to clarify the relationship between length of treatment and treatment outcome. Also of interest are studies to determine the roles of legal coercion, social supports and/or pressure, and other external factors that influence retention in treatment.

**Compliance in treatment.** Research indicates that during-treatment performance is predictive of post-treatment outcomes. New studies to examine strategies to improve treatment performance by reducing problematic use of alcohol and other drugs, by improving participation in treatment, or by improving compliance with other treatment program goals are encouraged. Investigations may also focus on improving the operation or organization of treatment programs to increase compliance and retention.

**Studies may be of single interventions** such as behavioral contingencies, combinations of interventions, program structure interventions combining targeted services and behavioral contingencies, and/or the use of medications in conjunction with program structure. Examples of program structure factors include negotiation of behavioral expectations (e.g., job search, participation in training), monitoring program-relevant behavior, participation in individual and group counseling or therapy as a condition for remaining enrolled in treatment, tracking and outreach to reduce treatment dropout, and linking social incentives such as social services or job training/placement to treatment enrollment and participation.

**Strategies to increase compliance** may include improving the staff/patients therapeutic relationship, assessing and meeting patient needs (e.g., medical/dental care, child care), improving the effectiveness of drug abuse counselors in meeting patient needs, and pharmacological and behavioral strategies alone or in combination. Investigators may wish to consider compliance strategies in patient subgroups based on diagnostic criteria and stages of recovery. Research that examines fundamental questions of program philosophy and patient-treatment interactions (including matching) are encouraged.

#### Specific Areas of Interest

Research priorities include the need to characterize better the individuals who stay in or leave treatment, to examine the decision process leading to remaining in treatment, and to assess program factors that may inhibit or facilitate treatment compliance. Also relevant are the potential influences of concurrent psychiatric and other medical disorders (e.g., AIDS) on treatment retention and compliance.

Research is needed on how patient personality, perceptions, expectations, and beliefs affect treatment retention and the effect of program organization, leadership, and context on the retention process. The role social networks play in the decision to remain in treatment and in compliance with treatment also should be explored.

Since drug dependence is a chronic relapsing disorder, more needs to be learned about persistent drug-induced neuropsychological changes that may be involved in leaving treatment or failures to comply with treatment. Also, there should be study of the effects of drug availability and other environmental factors on retention.

To clarify intrapersonal and environmental factors associated with treatment retention and compliance, studies of untreated drug dependent persons, as well as those in treatment, are strongly encouraged. Thus, epidemiological and ethnographic studies are needed to complement what can be learned through studies of interventions. Research on the natural history of drug disorders should be particularly helpful in clarifying the role of a variety of treatments in retention as well as factors associated with compliance. To facilitate this research, methodological approaches for assessing the long-term course of drug disorders need to be refined.

Archival and secondary analyses are encouraged to exploit the potential of existing data sets. Development of compatible data bases across programs are encouraged to facilitate replication across settings, with different populations, and over time.

Examples of research areas identified above include the following:

- o Factors associated with treatment retention and compliance (e.g., patient personality, perceptions, expectations, and beliefs) should be explored explicitly in treatment research studies. Comorbidity studies could be informative.
- o The role of social networks in affecting treatment retention and compliance should be studied. Examination of gender, ethnic, and educational differences and examination of differences in social competence are particularly important.
- o The characteristics of individuals who stay in or leave treatment should be studied to determine how they differ and possible ways in which those who leave treatment can be induced to remain in treatment. The decision-making process leading to decision to leave treatment--including the roles of factors such as drug-related neuropsychological deficits, family members, and coercion in deciding to seek treatment--should be studied.
- o Treatment retention failures should be studied to determine why treatment retention does not occur. This should include why persons fail to invest in treatment.
- o The effect of program organization, leadership, and context on treatment retention should be studied. Research should include studying the impact of program type (e.g., directive-nondirective, medical-normedical orientation, residential-nonresidential), perceived staff caring (the so-called "smile factor"), and cultural aspects of the program (race, ethnicity, language) on retention.
- o Better methods to assess and evaluate the probability of leaving treatment are needed (e.g., employing



measures of drug craving, drug availability, stage(s) in drug abuse history, cognitive deficits, availability of support systems).

o Neuropsychological factors, including those that are drug induced, may increase the likelihood in some persons to leave treatment and these factors should be studied. Cognitive deficits of drug abusers in treatment may preclude treatment compliance and their role in the treatment retention process needs to be assessed.

#### Cross-Institute/Intra-Institute Areas of Interest

Projects may be submitted under this announcement that address issues in common with, for example, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute of Mental Health (NIMH), and various programs within NIDA. Also, applicants may wish to collaborate with the Center for Substance Abuse Treatment (CSAT) or the Center for Substance Abuse Prevention (CSAP) grantees who deal with the types of environmental and social factors addressed by this announcement. It is conceivable that an applicant could carry out the research in the context of a CSAP Community Partnership grant, a CSAT Target Cities grant, a CSAP High Risk Youth grant or other initiative. This would have the benefit of providing a potential applicant with a pool of patients and a primed community. Preapplication consultation with the individual listed below is strongly encouraged. Applications are considered for acceptance and assigned according to standard NIH/PHS referral guidelines.

#### International Comparative Studies

It is recognized that some treatment research issues related to such areas as retention in treatment, program completion, and compliance with treatment expectations lend themselves to comparative multi-site study, especially where environmental differences and available treatment options are concerned. Well-designed comparative multi-site studies may include program sites in foreign countries, provided that the foreign program site is justified in terms of the research objectives. Such studies may include a collaborating scientist or clinical researcher affiliated with the foreign program sites. However, foreign institutions are not eligible for FIRST awards (R29s).

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.



#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. The receipt dates for applications for AIDS-related research are found in the PHS 398 instructions.

Application kits are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in Item 2a of face page of the application.

FIRST award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original and five permanent, legible copies of the PHS 398 form must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

The Division of Research Grants (DRG), NIH, serves as a central point for receipt of applications for most discretionary HHS grant programs. Applications received under this announcement will be assigned to an initial review group (IRG) in accordance with established PHS referral guidelines. The IRGs, consisting primarily of non-Federal scientific and technical experts, will review the applications for scientific and technical merit in accordance with the standard NIH peer review procedures. Notification of the review recommendations will be sent to the applicant after the initial review. Applications will receive a second-level review by an appropriate national advisory council, whose review may be based on policy considerations as well as scientific merit. Only applications recommended for further consideration by the council may be considered for funding. Small grants (R03s) do not receive a second level review.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to the Institute/Center/Division. The following will be considered when making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Frank M. Tims, Ph.D.  
Treatment Research Branch  
Division of Clinical Research  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 10A-30  
Rockville, MD 20857  
Telephone: (301) 443-4060

Direct inquiries regarding fiscal issues to:

Mrs. Shirley A. Denney  
Chief, Grants Management Branch  
National Institute on Drug Abuse  
5600 Fishers Lane, Room 8A-54  
Rockville, MD 20857  
Telephone: (301) 443-6710

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.279. Awards are made under authorization of the Public Health Service, Sections 301 and 405, and administered under PHS policies and Federal Regulations at Title 42 CFR 52, Grants for Research Projects, Title 45 CFR Part 74 & 92, Administration of Grants, and 45 CFR Part 46, Protection of Human Subjects. Title 42 CFR Part 2, Confidentiality of Alcohol and Drug Abuse Patient Records may also be applicable to these awards. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

Sections of the Code of Federal Regulations are available in booklet form from the U.S. Government Printing Office.

Grants must be administered in accordance with the PHS Grants Policy Statement, (rev. 10/90), which is available from institutional offices of sponsored research.

NIH GUIDE, Volume 21, Number 44, December 11, 1992

PA: PA-93-29

P.T. 34; K.W. 0715075, 0785095, 0765033, 0411005, 0755030

National Institute of Diabetes and Digestive and Kidney Diseases

#### PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites research applications for studies related to Kidney Disease of Diabetes Mellitus (KDDM). This Program Announcement (PA) invites submission of individual research grant applications focusing primarily on basic research into the pathogenetic mechanisms of KDDM.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Kidney Disease of Diabetes Mellitus: Pathogenetic Mechanisms, is related to the priority area of diabetes and chronic disabling diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone (202) 783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit or non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Minority individuals and women are encouraged to apply. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) (R29) awards.

#### MECHANISM OF SUPPORT

Support of this program will be through the traditional NIH grant-in-aid research project grant (R01) and First Independent Research Support and Transition (FIRST) award (R29). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this announcement, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement. It should be noted that FIRST (R29) awards are restricted to domestic institutions only.

A maximum of three years may be requested for foreign awards. FIRST award applications should request five years. Annual awards will be made, subject to continued availability of funds and progress achieved.

Although this program is provided for in the financial plans of the NIDDK, the award of grants pursuant to this PA is contingent upon the availability of funds for this purpose. It is anticipated that the average size of an award made in response to this PA will be about \$180,000 per year including both direct and indirect costs; however, considerable variability around this average is expected.

#### RESEARCH OBJECTIVES

This PA is intended to encourage new fundamental studies of KDDM. The aim is to stimulate investigator-initiated research protocols designed to further the understanding of the pathogenetic mechanisms and genetic determinants of KDDM, as well as to address issues concerning risk factors, co-morbidity, and causes of excess incidence of diabetic end-stage renal disease (ESRD) in certain minority populations.

Kidney disease of diabetes mellitus (KDDM) continues to be the most frequent cause of ESRD in the USA and the largest single cause of renal disease. This is true for Caucasians, African Americans, Hispanics, and Native Americans. Even though progress has been made in understanding some of the mechanisms leading to the development of KDDM and its progression to ESRD, the pathogenesis of KDDM still remains largely undefined.

Examples of representative research topics that would be considered responsive to this solicitation include the following:

- o Characterization of the pathogenetic mechanisms and the genes associated with KDDM, including the role of the genes in the immune response in insulin-dependent diabetes mellitus (IDDM), and genetic and environmental determinants in non-insulin dependent diabetes mellitus (NIDDM).
- o Identification of the role, pathways, and interaction of biochemical and metabolic factors in KDDM.
- o Comparison of KDDM in IDDM vs NIDDM.
- o Biochemical characterization of the changes observed in glomerular basement membrane.
- o Morphologic and morphometric studies of, e.g., the glomeruli, including basement membrane thickening, extent of mesangial expansion, and quantitation of capillary surface area with disease progression.
- o Studies addressing risk factors and co-morbidity in KDDM.
- o Studies of the pathophysiology of hyperfiltration and its linkage to subsequent morphologic injury.

o Investigation of the possible causes of the excess incidence of KDDM in Blacks, Hispanics, and Native Americans, including genetic and environmental factors.

o Studies examining the etiology of KDDM including non-enzymatic glycation, aldose reductase activity, hyperinsulinemia, and hyperglycemia, that may serve as a model for understanding KDDM and other complications of diabetes.

#### SPECIAL REQUIREMENTS

Interdisciplinary approaches may be needed and are encouraged for these studies. For example, collaborations among the following disciplines may be productive: molecular and cell biology, genetics, immunology, pathology, biochemistry/metabolism, nephrology, endocrinology, physiology, and pharmacology.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Item 4 (Research Design and Methods) of the Research Plan and summarized in Item 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics.

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention [and preventive strategies], diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned without review.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev.9/91) is to be used in applying for these grants. The form is available from most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

The PA title and number must be typed on line 2a of the face page of the application form and check the YES box.

Submit a signed, typewritten original of the application, including the Checklist, and five signed, exact photocopies, in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

FIRST (R29) award applications must include at least three sealed letters of reference attached to the face page of the original applications. FIRST (R29) award applications submitted without the required numbered of reference letters will be considered incomplete and will be returned without review.



The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, it is allowable to submit the same project as both an R01 and as a component project of a program project. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications previously reviewed. Such applications must not only include an introduction addressing the previous critique, but also be responsive to this PA.

#### REVIEW CONSIDERATIONS

Applications received in response to this PA will be assigned to an initial review group and to an awarding Institute/Center for possible funding on the basis of established PHS referral guidelines. A review for scientific and technical merit will be conducted by an initial review group convened by the DRG in accordance with the standard NIH peer review procedures. Following this review, the applications will be given a secondary review by the National Diabetes and Digestive and Kidney Diseases Advisory Council or the corresponding Advisory Council/Board of another funding component (unless the application is not recommended for further consideration by the initial review group).

Review criteria for application submits in response to a PA are generally the same as those for unsolicited research grant applications. Review criteria include:

- o Scientific, technical, or medical significance and merit specific to the objectives of the PA and originality of the proposed research
- o Appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research
- o Qualifications and research experience of the Principal Investigator and staff, particularly but not exclusively in the area of the proposed research
- o Availability of resources necessary to perform the research
- o Appropriateness of the proposed budget and duration in relation to the proposed research

#### AWARD CRITERIA

Applications received in response to this PA will compete for available funds with other applications recommended for funding. The following will be considered in making funding decisions:

- o quality of the proposed project as determined by peer review,
- o availability of funds, and
- o program balance among research areas of the announcement.

#### INQUIRIES

NIDDK staff are available for consultation concerning application development before or during the process of preparing an application. Potential applicants are advised to contact NIDDK staff as early as possible for information or assistance in initiating the application process and developing an application.

Direct inquiries regarding programmatic issues to:

Gladys H. Hirschman, M.D.  
Director, Chronic Renal Diseases Program  
Division of Kidney, Urologic and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A-07  
Bethesda, MD 20892  
Telephone: (301) 496-8218

or

Charles A. Wells, Ph.D.  
Director, Diabetes Complications Program  
Division of Diabetes, Endocrinology and Metabolic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 622  
Bethesda, MD 20892

Direct inquiries regarding fiscal matters to:

Aretina D. Perry  
Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 639  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.849 and 93.847. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public



## RESEARCH ON RAYNAUD'S PHENOMENON AND SYSTEMIC SCLEROSIS

NIH GUIDE, Volume 21, Number 44, December 11, 1992

PA NUMBER: PA-93-30

P.T. 34; K.W. 1002004, 0765033

National Institute of Arthritis and Musculoskeletal and Skin Diseases

### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites research grant applications for studies of basic biological and clinical aspects of Raynaud's phenomenon, focusing particularly on microvascular control mechanisms, collagen synthesis, and other aspects of fibroblast biology, endothelial cell function, and immunological abnormalities associated with Raynaud's phenomenon. The goal of this program announcement (PA) is to promote research that contributes to the understanding the pathogenesis of Raynaud's phenomenon and its relationship to other pathogenetic mechanisms in systemic sclerosis.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Research on Raynaud's Phenomenon and Systemic Sclerosis, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

### ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private institutions, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) awards (R29).

### MECHANISM OF SUPPORT

Applications are requested under the following mechanisms: traditional research grants (R01), FIRST awards (R29). Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also.

### RESEARCH OBJECTIVES

The goal of this PA is to encourage research that will elucidate the relationship between Raynaud's phenomenon and systemic rheumatic illness. Raynaud's phenomenon consists of intermittent blanching, reactive hyperemia, and cyanosis of fingers, toes, ears, and nose in response to cold, emotion, and other external events. More than 90 percent of patients with scleroderma (systemic sclerosis) and approximately 25 percent of patients with systemic lupus erythematosus develop Raynaud's phenomenon, often as the first symptom, but the relationship between this abnormality and the associated rheumatic illness remains unknown. Recent studies have suggested that the primary abnormality may reside in control mechanisms for microvascular blood flow, endothelial cell injury, or pathologic biology of endothelial cells or fibroblasts. In scleroderma, Raynaud's phenomenon is closely associated with excessive skin fibroblast synthesis of skin collagen. Several autoantibodies occur in patients with scleroderma and with systemic lupus erythematosus; whether these autoantibodies cause, follow, or are unrelated to the occurrence of Raynaud's phenomenon is unknown.

Research proposed in response to this Program Announcement may be at any level of biological organization, but must in some way address the pathophysiology of Raynaud's phenomenon and/or its relationship to systemic sclerosis or other rheumatic disease. Possible topics include, but are not limited to, the following:

- o Up- and down-regulator mechanisms of microvascular blood flow;
- o Neurogenic mechanisms in microcirculatory abnormalities;
- o Immunologically-mediated endothelial cell injury;
- o Control mechanisms of fibroblast function as it relates to the occurrence of scleroderma; and
- o Relationship of specific autoantibodies to Raynaud's phenomenon.

### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies,

a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the PA must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by initial review groups (study sections) of the Division of Research Grants (DRG), NIH, in accordance with the standard NIH peer review procedures.

Following scientific-technical review, the applications will receive a second-level review by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council or by other relevant advisory boards and/or councils.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to NIAMS. The following will be considered in making funding decisions:

- o quality of the proposed project as determined by peer review;
- o availability of funds; and
- o program balance among research areas of the announcement.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Director, Arthritis Program  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 405  
Bethesda, MD 20892  
Telephone: (301) 402-3340

Direct inquiries regarding fiscal matters to:

Diane M. Watson  
Chief, Grants Management Branch  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 732A  
Bethesda, MD 20892  
Telephone: (301) 402-3352

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### RESISTANCE TO ANTIVIRALS TARGETED TO HUMAN IMMUNODEFICIENCY VIRUS

NIH GUIDE, Volume 21, Number 44, December 11, 1992

PA NUMBER: PA-93-31

P.T. 34; K.W. 0715008, 0740012, 0765012, 0755060

National Institute of Allergy and Infectious Diseases

Application Receipt Dates: January 2, May 1, September 1, 1993

#### PURPOSE

This Program Announcement (PA) is designed to stimulate research to: (1) elucidate mechanisms of Human Immunodeficiency Virus (HIV) drug resistance, (2) determine the effects of viral drug resistance in lentivirus pathogenesis, (3) identify improved methods to screen for drug resistant HIV and animal lentivirus variants, and (4) design and evaluate novel therapies for treating or preventing drug resistance, utilizing in vitro and animal model systems as applicable.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Resistance to Antivirals Targeted to HIV, is related to the priority area of HIV infection. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000: (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

This PA solicits R01 and R29 applications. While no funds have been set aside specifically for supporting applications submitted in response to this PA, the NIAID regards additional quality research in this area to be of high programmatic priority. The total project period for awards made in response to this PA will not exceed four years for domestic institutions and three years for foreign institutions. If an R29 application is submitted, three reference letters are required to be submitted with the application and stapled to the face page of the original application.

#### RESEARCH OBJECTIVES

##### Background

The Developmental Therapeutics Branch (DTB), Basic Research and Development Program (BRDP), Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID) supports basic and applied research grants leading to the discovery of new therapies for the treatment of HIV infection and the opportunistic infections (OIs) associated with AIDS. This goal is accomplished through: (1) management of investigator-initiated research for HIV; (2) fostering of innovative, multidisciplinary efforts leading to the discovery and design of new anti-HIV and anti-OI therapies through the National Cooperative Drug Discovery Group programs for treatment of HIV infection (NCDDG-HIV) and for treatment of the OIs associated with AIDS



(NCDG-01); and (3) preclinical drug development contract resources to confirm activity of anti-HIV and anti-OI compounds, and to evaluate combination and immune-based therapies in vitro and in animal models. The DTB released a Request for Applications (RFA) entitled "Drug Resistance and the Human Immunodeficiency Virus" in 1989. Applications funded in response to that RFA focused predominantly on methodologies for detecting HIV variants with reduced susceptibility to antivirals.

During the past few years, our understanding of the emergence of drug-resistant HIV has increased dramatically. For example, diminished in vitro susceptibility of HIV clinical isolates from patients undergoing treatment with AZT for as few as six to twelve months is well documented. Associated with this phenotype of reduced susceptibility to AZT is a characteristic pattern of genetic alterations at codons 41, 67, 70, 215, and 219 of reverse transcriptase (RT) that appear to emerge in a temporal fashion conferring progressively increasing resistance. The complex interplay among these mutations as evidenced by (1) the disappearance of the codon 70 mutation in sequential clinical isolates that show increased resistance and (2) the stability of the mutation at codon 215 in isolates from patients switched to ddI therapy that have reverted to AZT susceptibility is not well understood. The precise mechanism by which these mutations confer the resistant phenotype in cell culture remains unknown.

More recently, a decrease in in vitro sensitivity to ddI of HIV isolates obtained from patients who changed to ddI therapy after prolonged treatment with AZT has been reported. An initial report describing resistance to ddC in one patient has also appeared. In addition, preliminary results from clinical trials indicate that HIV drug resistance to several non-nucleoside RT (NNRT) inhibitors, as determined in vitro, develops rapidly in patients. Novel mutations in HIV RT that correlate with in vitro resistance to ddI, ddC and the NNRT inhibitors have been identified in clinical isolates. Introduction of these specific mutations into the genetic background of a replication competent, fully susceptible virus confers a resistant phenotype that mimics the susceptibility profile of the original clinical isolates.

In summary, characteristic patterns of mutations in HIV-1 RT have been identified at the molecular level in resistant variants and genetic signatures appear to be distinct for each inhibitor or class of inhibitors. These observations notwithstanding, the exact mechanism(s) by which the resistant phenotype is manifested in vivo via these alterations is not known, and the clinical significance of HIV-related drug resistance remains unknown at this time.

#### Research Scope

Molecular, enzymatic and biologic effects of drug resistance: Given the precedence of resistance to several nucleoside analogs and to NNRT inhibitors in clinical isolates, it is expected that resistance to inhibitors directed against other viral targets is likely to occur. With the introduction of anti-HIV agents other than RT inhibitors into clinical trials and the preclinical development of others, studies involving therapeutic modalities directed against non-RT targets, e.g., protease, TAT, myristoylation, as well as against RT, are urgently needed.

Crucial clinical studies to determine whether or not emergence of drug resistant variants is correlated with disease progression are underway. Of equal importance are studies that decipher the molecular, enzymatic and biological aspects of HIV drug resistance that can serve as the basis for developing therapeutic strategies to overcome or delay the emergence of drug resistant HIV in the clinic. While clinical relevance awaits further corroboration, research focussed on understanding the mechanisms underlying resistance and the biological properties of the resistant virus that are implicated in disease progression is encouraged. As mentioned above, in spite of the identification of characteristic genetic alterations conferring a drug resistant phenotype on HIV, the precise mechanism(s) by which these mutations mediate their enzymatic and biological impact on the resistant phenotype is unknown. The following areas of research are particularly encouraged:

- o Elucidation of the basis for the apparent inability of cell-free assays to distinguish RT purified from AZT-resistant vs. AZT-sensitive isolates may shed additional light on this dilemma. This is contrasted by retention of the drug resistant phenotype in RT purified from NNRT- resistant HIV.
- o Structure/function studies of drug resistant viral targets in the presence and absence of drug may also contribute to delineating the mechanisms by which genetic alterations result in loss of drug effect.
- o The biological effects the genetic alterations conferring the resistant phenotype have on the properties of the virus in terms of its pathogenicity and capacity to accelerate or attenuate disease progression are not well studied. Information is also incomplete regarding the relationship between HIV variants capable of forming syncytium upon cocultivation of infected patient peripheral blood lymphocytes with MT-2 cells, viral drug resistance and clinical progression.
- o The effect of drug resistance on viral transmission needs to be elucidated. If drug resistant HIV variants are transmitted, is the frequency comparable to that of their drug sensitive counterparts?

Phenotypic and genotypic detection of drug resistance: Sensitive and reproducible methods for (1) detection of drug resistant HIV mutants, including primary isolates within phenotypic mixtures and (2) quantitation of levels of drug resistance and proportion of resistant HIV variants are urgently needed to delineate the mechanism(s) and impact of resistance and to predict the efficacy of new therapies. Methods for the expansion of primary HIV isolates to adequate titers with minimal selection for specific viral variant(s) are also critical. Recent evidence suggests that passage of clinical isolates in cell lines may rapidly select for specific genotypes.

#### Specifically

- o Additional culture systems should be developed that closely model the in vivo situation. Currently, assays utilizing fresh peripheral blood mononuclear cells (PBMC) have received the predominant focus. However, variable infectability of donor cells may preclude the standardization of this assay system. Methods for expansion of primary HIV isolates to adequate titers with minimal selection for specific viral variant(s) are also critically needed.



o Genotypic assays also suffer from certain limitations, particularly those imposed by the possibility that the genetic signature of resistance associated with a specific therapeutic may not yet be comprehensive. Technical difficulties also exist in designing polymerase chain reaction primers that can accurately, specifically, and reproducibly amplify the associated mutations.

Because of these current limitations and deficiencies in evaluating HIV drug resistance, development of novel and/or validation of existing assays to measure viral susceptibility to antivirals is/are strongly encouraged. For example, innovative, highly sensitive biophysical methods recently developed may be modified and implemented to identify alterations previously undetectable at the protein level that correspond to mutations conferring the resistant phenotype. Such changes may represent markers for HIV resistance to drugs or may, themselves, be directly responsible for the drug resistant phenotype.

Animal models of drug resistance: Development and implementation of relevant animal models of lentivirus infection are critically needed to address these resistance issues. Efforts to establish an animal model of viral drug resistance may include development of protocols for detection and quantitation as well as expansion of isolates, as the problems addressed above for HIV-specific susceptibility assays are likely to be similar. Animal models of lentiviral infection (e.g., SIV and FIV) of potential relevance are available. Thus, systematic evaluation of virus isolates from drug-treated animals may define an animal model that parallels documented resistance in HIV-infected patients. Once developed, such model(s) may be exploited for assessing drug therapy and drug resistance.

Novel strategies for circumventing HIV drug resistance: The ultimate goal of these studies is to design novel strategies to circumvent and/or delay the development of viral drug resistance. As an example, one approach can focus on highly conserved functional domains identified in several HIV proteins (RNA-dependent and DNA-dependent activities, and RNaseH and RNaseD activities of RT; transactivation, nuclear-targeting, and RNA/protein binding activities of Tat). The observation that these domains are spared from sequence variations suggests that most mutations in these regions would be lethal to the virus and, therefore, to have no or minimal consequence on drug treatment. This and other research objectives include, but are not limited to:

- o Exploiting other viral targets believed to be essential for viral survival, and thus incompatible with resistance-conferring mutations
- o Investigating combination therapies designed to inhibit more than one distinct step in the HIV infectious cycle that may delay the development of viral drug resistance by virtue of a multipronged action
- o Designing studies to reduce the overall rate at which HIV mutates. While not specifically addressed in this PA, evaluation of the role of host-mediated processes in the resistant phenotype may also provide insight into developing new therapeutic approaches.

The rationale for any potential approach should first be tested and analyzed in an appropriate in vitro system, if applicable. For example, a new therapeutic regimen may be evaluated for its effect on in vitro emergence of resistant HIV variants. Alternatively, a novel therapeutic strategy may be tested for its activity against established resistant mutants. Subsequent evaluation of new drug strategies in relevant animal models should yield important information on the applicability of the proposed strategies to the clinical setting. The approaches outlined above are examples of potential research directions bearing on the emergence of HIV drug resistance and are not intended to be comprehensive.

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

NIH policy is that applicants for NIH clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Items 1-4 of the Research Plan AND summarized in Item 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research involving human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be deferred until the information is provided.

Peer review will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in the study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on grant application form PHS 398 (rev. 9/91). Receipt dates are January 2, May 1, and September 1.

Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in Section 2a on the face page of application and the "YES" box marked.

The completed original application and five legible copies must be sent or delivered to

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

#### REVIEW PROCEDURES

Applications in response to this announcement are expected to be assigned to the NIAID. However, whenever there is inter-institute programmatic overlap in the proposed research, the PHS Referral Guidelines will prevail in the assignment of applications to the different institutes. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Applications focusing on AIDS will be assigned to study sections constituted to review AIDS-related grant applications. Following scientific-technical review, the applications will receive a second-level review by an appropriate national advisory council. For AIDS-related applications, the earliest award date for successful applications will be no more than six months from the receipt date.

#### AWARD CRITERIA

Applications will compete for available funds with all other approved applications. The following criteria will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review
- o Availability of funds
- o Program balance among research areas of the announcement.

Applications from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may identify the GCRC as a resource for conducting the proposed research by including a letter of agreement from either the GCRC program director or the principal investigator.

#### INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries of a scientific nature to:

Roberta Black, Ph.D.  
Basic Research and Development Program, Division of AIDS  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 2C12  
Bethesda, MD 20892  
Telephone: (301) 496-8197  
FAX: (301) 480-5703/402-3211

Direct inquiries regarding fiscal matters to:

Ms. Jane Unsworth  
Chief, AIDS Grants Management Section  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B22  
Bethesda, MD 20892  
Telephone: (301) 496-7075  
FAX: (301) 480-3780

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, 93.856 - Microbiology and Infectious

Diseases Research and 93.855 - Immunology, Allergy and Transplantation Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### INSTITUTIONAL RESEARCH TRAINING IN ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

NIH GUIDE, Volume 21, Number 44, December 11, 1992

PA NUMBER: PA-93-32

P.T. 44; K.W. 0715020, 0705050, 0715140, 0715010, 0715170, 0715185, 0720005 1002004, 0790000, 0710070

National Institute of Arthritis and Musculoskeletal and Skin Diseases

#### PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites applications to develop or enhance research training for individuals who conduct basic and clinical research on the tissues and diseases within its mandate. The proposed training plan may include short-term training for health professionals as well as full time predoctoral and post-doctoral positions. The purpose of this announcement is to ensure a cadre of well trained scientists interested in pursuing research careers in areas relevant to the mission of the NIAMS.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement, Institutional Research Training Awards in Arthritis and Musculoskeletal and Skin Diseases, is related to the priority areas of chronic disabling conditions and physical activity and fitness. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, non-profit, private and public institutions to support research training programs. The applicant institution must have, or be able to develop, the staff and facilities required for the proposed program. The training program director at the institution will be responsible for the selection and appointment of trainees to receive support and for the overall direction of the program.

The individuals to be trained on a National Research Service Award (NRSA) training grant must be citizens or non-citizen nationals of the United States or have been lawfully admitted for permanent residence (i.e., in possession of the Alien Registration Receipt Card I-551 or I-151) at the time of appointment. Individuals on temporary or student visas are not eligible. NRSA research training grants may not be used to support studies leading to the M.D., D.O., D.D.S., D.V.M., or other similar health-professional degree. Individuals holding an M.S., a Ph.D., or M.D./Ph.D. or an equivalent graduate level research degree, are not eligible for short term training positions. Programs able to provide postdoctoral training to both M.D.s and Ph.D.s are encouraged. Institutions are encouraged to develop multi-year plans that provide strong research training for health professionals, while cognizant of requirements for board certification.

#### MECHANISM OF SUPPORT

The mechanism of support for this program announcement will be the NRSA institutional training grant (T32). Institutions may request support for predoctoral students, postdoctoral trainees, and short-term research training. Stipends will be awarded at levels commensurate with NIH policy at the time of award and may be supplemented from non-Federal sources. Training related expenses, tuition and fees, and travel expenses may also be requested for trainees, although the levels vary depending on the type of training to be supported. Postdoctoral trainees should be appointed for at least two years.

#### RESEARCH OBJECTIVES

The NIAMS is committed to increasing the number of well-trained health professionals and basic scientists interested in conducting high quality research in areas of its mission and able to both compete successfully for NIH grant support and provide leadership in the areas of clinical research. The research program of training grant applications should be related to the mission of the NIAMS.

Major areas of interest to the NIAMS, with respect to institutional awards, include:

- o Arthritis and Other Rheumatic Diseases
- o Muscle Biology and Muscle Diseases
- o Musculoskeletal Diseases and Disorders, including Orthopaedic Research
- o Skin Biology and Skin Diseases
- o Bone Biology and Bone Diseases
- o Rheumatic Diseases in Children
- o Epidemiology of Arthritis, Bone, Muscle, and Skin Diseases
- o Multidisciplinary Approaches

Due to the complexity of the tissues and diseases, it is becoming increasingly clear that research excellence in arthritis, muscle biology, musculoskeletal disorders, bone and skin diseases requires interdisciplinary



approaches. Thus, the NIAMS encourages institutions to develop training programs that support individuals in acquiring expertise in several disciplines such as molecular biology, cell biology, structural biology, biophysics, immunology, developmental biology, genetics, and epidemiology. Additionally, research training programs may be strengthened by combining or crossing traditional departmental or specialty divisions.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

#### APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91). Application kits are available from most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

Prior to preparing an application, prospective applicants should consult the "National Research Service Award Guidelines for Individual Awards - Institutional Awards," available from most grantee offices of sponsored research and from the Office of Grants Inquiries at the address listed above. Applicants should note the "Modification of Existing Review Criteria for NRSA Institutional Research Training Grants" issued in the NIH Guide for Grants and Contracts, Vol. 21, No. 11, March 20, 1992. Institutional Research Training Grant Applications may be submitted on January 10, May 10, and September 10 of each year. Applications submitted in response to this announcement must be identified by typing PA-INSTITUTIONAL RESEARCH TRAINING IN NIAMS and PA-93-32 on line 2a of the face page, below the title of the project.

The typed original application and five signed exact single-sided photocopies must be submitted or delivered to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may identify the GCRC as a resource for conducting the proposed activity. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator should be included with the application.

#### REVIEW PROCEDURES

Upon receipt, applications will be reviewed initially by the Division of Research Grants (DRG) for completeness.



Incomplete applications will be returned to the applicant without further consideration.

All applications responding to this announcement that are assigned to the NIAMS will be reviewed for scientific and technical merit by the AMS initial review group (IRG), followed by a second level review by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council. Applications not recommended for further consideration by the IRG will not undergo secondary review. Applications assigned to Institutes/Centers other than the NIAMS will undergo a similar two-level review process within the designated Institute/Center.

Review criteria used by initial review groups in reviewing NRSA Institutional Training applications are given in the booklet "National Research Service Award Guidelines for Individual Awards - Institutional Awards," dated March 20, 1992, available from the Office of Grants Inquiries at the address listed under APPLICATION PROCEDURES.

#### AWARD CRITERIA

Applications will compete for available funds with other approved applications. The following will be considered in making funding decisions:

- o scientific and technical merit of the application as determined by peer review,
- o availability of funds, and
- o program balance.

#### INQUIRIES

For further information about these awards, contact:

Richard W. Lynn, Ph.D.  
Program Director  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 403  
Bethesda, MD 20892  
Telephone: (301) 402-3346

For administrative and fiscal matters, contact:

Diane Watson  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 732  
Bethesda, MD 20892  
Telephone: (301) 402-3352

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52, 45 CFR Part 74 and 42 CFR Part 66. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### ERRATA

#### RESEARCH USING THE UNITED STATES RENAL DATA SYSTEM

NIH GUIDE, Volume 21, Number 44, December 11, 1992

RFA: DK-93-12

P.T. 34; K.W. 0785095, 0755018

National Institute of Diabetes and Digestive and Kidney Diseases

This erratum is issued for Request for Applications DK-93-12, published in the NIH Guide for Grants and Contracts, Vol. 21, No. 40, November 6, 1992. The section MECHANISM OF SUPPORT should be amended with the addition of the following sentence:

"Each grant award will not be more than \$50,000 total cost per year (direct and indirect) for a maximum of two years."

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

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# NIH GUIDE

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## For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 21, No. 45  
December 18, 1992

RICHARD W. MURR.

\* 4018  
\*\*61350E\*\*

929 WILD FOREST DRIVE  
GAITHERSBURG MD 20878 0000





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*This publication is also available electronically to institutions via BITNET or INTERNET. Alternative access is through the NIH Grant Line using a personal computer. Contact Dr. John James at 301/496-7554 for details, or send an E-mail message to ZNS@NIHCU.*

*This is the final issue of the NIH Guide to Grants and Contracts for 1992. The next edition, Volume 22, Number 1, will be published on January 8, 1993. Have a Joyous New Year!*

HEREDITARY HEARING IMPAIRMENT RESOURCE REGISTRY

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFP AVAILABLE: NIH-DC-93-02

P.T. 34; K.W. 0715050, 1002019, 0780030

National Institute on Deafness and Other Communication Disorders

The National Institute on Deafness and Other Communication Disorders (NIDCD), National Institutes of Health, has a requirement to establish a Hereditary Hearing Impairment Resource Registry for the study of genetic hearing impairment and deafness, serving as a national resource for the biomedical research community. The contractor will encourage the direct enlistment of individuals and families in whom hearing impairment or deafness appears and who are willing to participate in genetic studies and the referral of individuals and families by their health care professionals. The contractor will collect and maintain clinical information on participants including specified medical, audiologic, demographic and epidemiologic variables. In addition, the contractor will encourage the pursuit of research on the genetic bases of hearing impairment and deafness by disseminating pertinent information to primary care physicians, otolaryngologists, audiologists and medical and molecular geneticists, and other biomedical scientists and health care professionals.

A three-year cost-reimbursement type contract is anticipated. The solicitation is scheduled for release on or about December 23, 1992, with proposals due on February 8, 1993. All responsible sources may submit a proposal that will be considered by the government.

**INQUIRIES**

Requests for copies of the solicitation are to be made in writing to:

John P. DeCenzo, Contracting Officer  
National Institute on Deafness and Other Communication Disorders  
Research Contracts Branch, DCG/OD  
Building 31, Room 1B44  
Bethesda, MD 20892  
Telephone: (301) 496-4487

DRUG DEVELOPMENT FOR TOXOPLASMOSIS ASSOCIATED WITH AIDS

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFP AVAILABLE: NIH-NIAID-DAIDS-93-25

P.T. 34; K.W. 0715008, 0715125, 0755060

National Institute of Allergy and Infectious Diseases

The Development Therapeutics Branch, Basic Research and Development Program, Division of AIDS of the National Institute of Allergy and Infectious Diseases (NIAID), is soliciting proposals from offerors with the capability to evaluate therapeutic agents for efficacy against *Toxoplasma gondii* encephalitis and latent toxoplasma infection in a rodent model. The contractor will evaluate therapeutic agents supplied or approved by the Project Officer for efficacy against *Toxoplasma gondii* in both rodent and in vitro models. During evaluations, the contractor may need to modify, improve or otherwise further characterize the rodent model and or in vitro model or develop other models to improve model utility in the evaluation of therapies. The Contractor may also be required to design alternative protocols and to conduct additional studies for detailed evaluation of promising therapeutic regimens.

Offerors must have in vivo and in vitro models available at the time of proposal. Past experience with animal models for Toxoplasmosis, the availability of the animals and strains of *Toxoplasma gondii*, and drug testing capability must be documented. This contract will be used to assist in the development of anti-infective therapies, to better understand the potential adverse health effects of such clinical trials.

This is an announcement for an anticipated Request for Proposal (RFP). The issuance of the RFP NIH-NIAID-DAIDS-93-25 will be on or about December 28, 1992, and proposals will be due by COB on or about March 24, 1993. It is anticipated that one cost-reimbursement contract will be awarded as a result of this solicitation and that the contract will have a five year period of performance.

**INQUIRIES**

To receive a copy of the RFP, provide this office with three self-addressed mailing labels. Telephone inquiries will not be honored and all inquiries must be in writing. Requests for the RFP are to be directed to:

Mr. Ross Kelley  
Contract Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3C-07  
6003 Executive Boulevard  
Bethesda, MD 20892  
Telephone: (301) 496-2509  
FAX: (301) 402-0972

A short-form version of the RFP will be provided first, which includes the Statement of Work, Reporting Requirements, and the Evaluation Criteria to be used for selection of the awardee. After examining this, a full-text version of the RFP must be requested, in writing, for those offerors interested in responding. FAX requests are acceptable for the full text version only. All proposals from responsible sources will be considered by the NIAID. This advertisement does not commit the Government to award a contract.

#### TUBERCULOSIS VACCINE DEVELOPMENT

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFA AVAILABLE: AI-93-02

P.T. 34; K.W. 0745020, 0715125, 0710070, 0785035, 0710030 0755010

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 19, 1993

Application Receipt Date: March 18, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY REQUEST THE RFA FROM THE CONTACT NAMES IN INQUIRIES.

#### PURPOSE

The Respiratory Diseases Branch of the Division of Microbiology and Infectious Diseases of the National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for research that will lead to the development of effective new vaccines for the prevention and control of tuberculosis. At present, a live attenuated strain of *Mycobacterium bovis*, Bacille Calmette Guerin (BCG), is the only vaccine available for protecting humans from tuberculosis. Protection elicited by BCG in controlled clinical trials has been variable. Applications that feature improvements to BCG will not be considered for funding under this RFA. However, applications that use BCG components in the development of a novel vaccine(s) are encouraged.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Tuberculosis Vaccine Development, is related to the priority areas immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, non-profit and for-profit research institutions; public and private organizations such as universities, colleges, hospitals, laboratories, units of State and local governments and eligible agencies of the Federal government. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) (R29) award. Applications from minority and women investigators are encouraged, as are applications from minority and women's institutions.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research project grant (R01), and the FIRST (R29) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing applications will compete with investigator-initiated applications and be reviewed according to customary review procedures.

#### FUNDS AVAILABLE

The estimated total funds (direct and indirect costs) available for the first year of the program is \$1,000,000. The NIAID plans to fund at least four R01s and/or R29s in fiscal year 1993. This level of support is dependent on availability of funds and receipt of a sufficient number of applications of high scientific merit.

#### RESEARCH OBJECTIVES

The long term goal of this initiative is to promote efforts to develop new, more effective vaccines not based on BCG to prevent and control tuberculosis. This will require innovative research approaches to develop candidate vaccine preparations that will elicit appropriate and protective functional responses. In order to achieve this objective, a focused effort on the basic biology of the mycobacterium and an understanding of the host response to natural infection is needed. Consistent with this, applicants are encouraged to develop innovative projects that address any of, though not limited to, the following areas:

- o Identification and characterization of components of *M. tuberculosis* that are immunogenic.
- o Identification and characterization of immunogens which elicit responses by the host during natural infection.
- o Isolation and characterization of relevant immunogen-coding sequences and their products.

o Characterization of the host response to natural infection and definition of the correlates of protective immunity.

Should an applicant have access to, or have already identified and prepared a novel candidate vaccine, this RFA would also encourage research in the area of:

- o Enhancement of the immunogenicity of candidate vaccine immunogens.
- o Development of animal model(s) for testing candidate vaccine immunogens.

The areas outlined are not intended to be all-inclusive nor are they all required.

#### SPECIAL REQUIREMENTS

NIAID program staff will organize annual meetings that Principal Investigators and other key members (as designated by the Principal Investigators) of the projects are encouraged to attend to discuss progress. Funds for travel to these meetings may be included in the budget.

#### STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to include minorities and women in study populations. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 19, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address and telephone number of the Principal Investigator, the identities of other key personnel and the participating institution, and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter in the review of the subsequent application, the information that it contains allows NIAID staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. Olivia Preble at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892 telephone (301) 496-7441. The deadline for receipt of applications is March 18, 1993. Applications for FIRST (R29) awards must include a least three sealed reference letters attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Further details on application procedures can be found in the RFA.

The typewritten, signed original application and three exact single-sided photocopies must be sent or delivered in one package to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, MD 20892\*\*

At the time of submission to the Division of Research Grants (DRG), two additional exact copies must be sent to Dr. Olivia Preble at the address listed under INQUIRIES.

Applications received after the deadline will be returned without review.

#### REVIEW CONSIDERATIONS

Upon receipt, applications and supporting material will be reviewed by the DRG for completeness and by the NIAID for responsiveness to the RFA. Incomplete applications will be returned without further consideration. If the application is not responsive to the RFA, NIAID staff will contact the applicant to determine whether to return the application or submit it for review in competition with unsolicited application at the next review cycle.

Applications may be triaged by an NIAID peer review group on the basis of relative competitiveness among the applications responding to the RFA. The NIAID will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications that are complete and responsive will be evaluated in accordance with standard NIH peer review criteria for scientific/technical merit by an appropriate review committee convened by the NIAID. The second level of review will be by the National Advisory Allergy and Infectious Diseases Council.

Review criteria for applications received in response to the RFA are generally the same as those for unsolicited applications.



## AWARD CRITERIA

The anticipated date of award is September 30, 1993.

The primary criterion for award will be the scientific and technical merit of the application as judged by peer reviewers and reflected in the priority score. Additional award criteria are the availability of funds and the receipt of a sufficient number of meritorious applications responding to the RFA.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify issues or questions from potential applicants is welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Dr. John Foulds, Tuberculosis Program Officer  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3A31  
Bethesda, MD 20892  
Telephone: (301) 496-5305  
FAX: (301) 496-8030

Direct inquiries regarding the review of applications and address the letter of intent to:

Dr. Olivia Preble  
Chief, Microbiology and Immunology Review Section  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C20  
Bethesda, MD 20892  
Telephone: (301) 496-8208  
FAX: (301) 402-2638

Direct inquiries regarding fiscal matters to:

Mr. Todd Ball  
Chief, Microbiology and Infectious Diseases Grants Management Section  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B35  
Bethesda, MD 20892  
Telephone: (301) 496-7075

## Schedule

Letter of intent date: January 19, 1993  
Application receipt date: March 18, 1993  
Scientific review date: July 1993  
Advisory Council date: September 1993  
Earliest award date: September 30, 1993

## AUTHORITY AND REGULATIONS

This program is supported under authorization of the Public Health Service Act, Sec. 301 (c), Public Law 78-410, as amended. The Catalogue of Federal Domestic Assistance Citation is Sec. 93.856, Microbiology and Infectious Diseases Research. Awards will be administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems review.

## BASIC BIOLOGY AND PATHOGENESIS OF HUMAN TUBERCULOSIS

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFA AVAILABLE: AI-93-03

P.T. 34; K.W. 0745020, 0715125, 0710070, 0785035, 0710030, 0755010

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 22, 1993  
Application Receipt Date: March 23, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY REQUEST THE RFA FROM THE CONTACT NAMES IN INQUIRIES.

## PURPOSE

The Respiratory Diseases Branch of the Division of Microbiology and Infectious Diseases and the Developmental Therapeutics Branch of the Division of AIDS of the National Institute of Allergy and Infectious Diseases (NIAID)

announces the availability of an RFA for research on the basic structural and functional biology and pathogenic mechanisms of *Mycobacterium tuberculosis*.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Tuberculosis Vaccine Development, is related to the priority areas immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, non-profit and for-profit research institutions, public and private organizations such as universities, colleges, hospitals, laboratories, units of State and local governments; and eligible agencies of the Federal government. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards. Applications from minority and women investigators are encouraged, as are applications from minority or women institutions.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research project grant (R01), and the FIRST (R29) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to this RFA may not exceed five years.

This RFA is a one-time solicitation. Future unsolicited competing applications will compete with investigator-initiated applications and be reviewed according to customary review procedures.

#### FUNDS AVAILABLE

The estimated total funds (direct and indirect costs) available for the first year of this program is \$1,000,000. The NIAID plans to fund at least four R01s and/or R29s in fiscal year 1993. This level of support is dependent on availability of funds and receipt of a sufficient number of applications of high scientific merit.

#### RESEARCH OBJECTIVES

Applications are encouraged that involve a coordinated multi-disciplinary approach to investigate *M. tuberculosis* and/or its interactions with its host (including animal models). Applications that involve an integration of basic and clinical sciences will be given favorable consideration. The aim of these efforts should be a greater understanding of mechanisms of pathogenesis, immune evasion, virulence factors or host response and/or lead to improvements in the diagnosis, treatment or prevention of tuberculosis. These areas may include, but are not limited to, the following:

- o Identify and characterize virulence factors important in the pathogenesis of tuberculosis.
- o Characterize the role(s) of tumor necrosis factor and other cytokines and soluble factors that affect the course of disease.
- o Develop improved in vitro or animal models for basic and applied studies.
- o Characterize cell surface antigens and describe their interactions with components of the host immune system.
- o Characterize the response of the host to natural infection and define the correlates of protective immunity.
- o Characterize immune mechanisms underlying successful inhibition of growth and persistence of tubercle bacilli in the body. Define the mechanisms by which *M. tuberculosis* persists in a quiescent state, and conditions under which reactivation of infection may occur.
- o Characterize mechanisms underlying drug resistance, particularly in MDRTB.
- o Develop improved methods for rapid, reliable identification of drug-sensitive and drug-resistant strains of *M. tuberculosis*, including MDRTB, in clinical specimens and in laboratory cultures.

#### SPECIAL REQUIREMENTS

NIAID program staff will organize annual meetings that Principal Investigators and other key members (as designated by the Principal Investigators) of the projects are encouraged to attend to discuss progress. Funds for travel to these meetings may be included in the budget.

#### STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to include minorities and women in study populations. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided. Applications without such documentation will not be accepted for review.

## LETTER OF INTENT

Prospective applicants are asked to submit, by January 22, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address and telephone number of the Principal Investigator, the identities of other key personnel and the participating institution, and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter in the review of the subsequent application, the information that it contains allows NIAID staff to estimate the potential review workload and to avoid possible conflicts of interest in the review.

The letter of intent is to be sent to Dr. Olivia Preble at the address listed under INQUIRIES.

## APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices for sponsored research or business offices and the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The deadline for receipt of applications is March 23, 1993. FIRST (R29) award applications must include three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Further details on application procedures can be found in the RFA.

## REVIEW CONSIDERATIONS

Upon receipt, applications and supporting material will be reviewed by the Division of Research Grants (DRG) for completeness and by NIAID staff for responsiveness to the RFA. Incomplete applications will be returned without further consideration. If the application is not responsive to the RFA, NIAID staff will contact the applicant to determine whether to return the application or submit it for review in competition with unsolicited application at the next review cycle.

Applications may be triaged by a peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by an appropriate peer review group convened by the NIAID. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council.

Review criteria for applications received in response to an RFA are generally the same as those for unsolicited applications.

## AWARD CRITERIA

The primary criterion for award is scientific and technical merit of the application as judged by peer review and reflected in the priority score. Other criteria are availability of funds and the number of meritorious applications received in response to the RFA. The anticipated date of award is September 1993.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify issues or questions from potential applicants is welcome.

Direct requests for the RFA and inquiries regarding programmatic issues to:

Dr. John Foulds, Tuberculosis Program Officer  
Respiratory Diseases Branch  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 3A31  
Bethesda, MD 20892  
Telephone: (301) 496-5305  
FAX: (301) 496-8030

Direct inquiries regarding the review of applications and send the letter of intent to:

Dr. Olivia Preble  
Chief, Microbiology and Immunology Review Section  
Scientific Review Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C20  
Bethesda, MD 20892  
Telephone: (301) 496-8208  
FAX: (301) 402-2638

Direct inquiries regarding fiscal matters to:

Mr. Todd Ball  
Microbiology and Infectious Diseases Grants Management Section  
Grants Management Branch  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B35  
Bethesda, MD 20892  
Telephone: (301) 496-7075

The mailing address for sending applications, letters of intent, or other correspondence to NIAID staff in the Solar Building is the central mailing address for the NIH. Applicants who use express mail or a courier service are advised to follow the carrier's requirements for showing a street address. The address for the Solar Building is:

6003 Executive Boulevard  
Rockville, MD 20852

#### Schedule

Letter of intent date: January 22, 1993  
Application receipt date: March 23, 1993  
Scientific review date: July 1993  
Advisory Council date: September 1993  
Earliest award date: September 30, 1993

#### AUTHORITY AND REGULATIONS

This program is supported under authorization of the Public Health Service Act, Sec. 301 (c), Public Law 78-410, as amended. The Catalogue of Federal Domestic Assistance Citation is Sec. 93.856, Microbiology and Infectious Diseases Research. Awards will be administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems review.

#### PHASE I TRIALS OF NEW ANTI-CANCER AGENTS

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFA AVAILABLE: CA-93-07

P.T. 34; K.W. 0755015, 0715035, 0740020, 0710100

National Cancer Institute

Letter of Intent Receipt Date: January 22, 1993  
Application Receipt Date: March 23, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Cancer Treatment (DCT), National Cancer Institute (NCI) invites cooperative agreement (U01) applications from single institutions wishing to perform Phase I trials of promising anti-cancer agents in patients with cancer refractory to currently available therapy and to conduct laboratory studies in support of the clinical trials such that their conduct leads to a greater understanding of the relationship between drug administration and biological changes in patients. It is expected that the application from any one institution will focus on studies of one or more classes of agents, reflecting the interest, expertise, and experience of the applicant investigators. Patients should be treated only at the applicant institution, although support for laboratory studies may be conducted by collaborators at other institutions.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Phase I Trials of New Anti-Cancer Agents, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202/783-3238).

#### ELIGIBILITY REQUIREMENTS

Domestic for-profit and non-profit organizations such as universities, colleges and hospitals and governments and their agencies are eligible to apply. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

Support of this program will be through the cooperative agreement (U01), an assistance mechanism in which substantial NCI programmatic involvement with the recipient during performance of the planned activity is anticipated. The nature of NCI staff involvement is described in the RFA. Applicants will be responsible for the planning, direction, and execution of the proposed project. Except as otherwise stated in this RFA, awards



This RFA is a one-time solicitation. However, if it is determined that there is a sufficient continuing program need, the NCI will invite recipients of awards under this RFA to submit competitive continuation cooperative agreement applications.

#### FUNDS AVAILABLE

Approximately \$2,000,000 in total costs per year for four years will be committed to specifically fund applications submitted in response to this RFA. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. It is anticipated that six to eight awards will be made. The total project period for applications submitted in response to the present RFA may not exceed four years. The earliest feasible start date for the initial awards will be December 1, 1994. Although this program is provided for in the financial plans of the NCI, the award of cooperative agreements pursuant to this RFA is contingent upon the availability of funds for this purpose.

#### RESEARCH OBJECTIVES

##### Background

Phase I clinical trials have as their objectives the characterization of drug toxicity, maximally tolerated dose, pharmacokinetics, and biological effects (pharmacodynamics) of drugs. These anti-cancer agents have traditionally been obtained either from the NCI drug development program or through collaborative drug development agreements with the pharmaceutical industry. Recent advances in understanding of the pathobiology of malignancy are leading to the development of a wide range of novel anti-cancer therapeutic agents that require Phase I testing. Furthermore, mechanisms of action of these new anti-cancer agents available for clinical study include not only the mediation of anti-cancer effects through cytotoxic mechanisms, but also through growth inhibition by interruption of specific oncogene-associated biochemical functions, inhibition of protein synthesis through targeted toxins, induction of differentiation and/or programmed cell death (apoptosis), and through anti-tumor angiogenesis. In addition, new strategies to overcome resistance to conventional cancer therapeutic approaches are also of interest.

In addition to the funding assistance offered to the investigator(s) by this RFA, NCI may sponsor (in the FDA sense) or co-sponsor the agents under development. This will increase the likelihood that agents will be further developed so that they will ultimately be broadly available for use in cancer treatment and will accelerate the time frame in which this process would occur.

##### Research Goals and Scope

The aims of this initiative are: (1) to provide support for Phase I trials of promising new anti-cancer agents in cancer patients; and (2) to provide support for complete pharmacokinetic, pharmacodynamic, and other important laboratory correlative studies in cancer patients receiving these anti-cancer agents. The laboratory studies should be in support of the clinical trial, such that their conduct leads to a greater understanding of the relationship between drug administration and biological changes in patients.

Specific objectives and scientific approaches will be investigator-originated and should reflect the creativity and capability of the investigators. This RFA provides an opportunity for clinical and laboratory investigators within an institution to develop a program in drug development that utilizes the strengths of pre-existing basic scientific expertise and available clinical resources.

Each Phase I awardee institution will be expected to complete an average of two to three Phase I trials per year, with each trial encompassing 20-40 patients. Each applicant institution is responsible for coordination of protocol development and submission, study conduct, quality control, data management and analysis, adherence to NCI requirements for investigational agents, adherence to FDA/DHHS regulations, and performance reporting of data from the Phase I trials. For Phase I trials with NCI-sponsored investigational agents, the NCI has contracted for a Clinical Trials Monitoring Service (CTMS) to document regulatory compliance, to maintain a computerized data base of the biweekly Phase I investigator data submissions, and to produce periodic routine reports of the results and special reports as necessary. The awardee institution's source documentation will be reviewed on-site three times per year by the CTMS.

#### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by January 22, 1993, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, it is requested in order to provide an indication of the number and scope of applications to be reviewed.

The letter of intent is to be sent to:

David R. Parkinson, M.D.  
Chief, Investigational Drug Branch  
Cancer Therapy Evaluation Program  
National Cancer Institute  
Executive Plaza North, Room 734  
Bethesda, MD 20892  
Telephone: (301) 496-5223  
FAX: (301) 480-4663

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for cooperative agreements. These forms are available at most institutional offices of sponsored research; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441; and from the NCI Program Director named below.

Applications must be received by March 23, 1993. If an application is received after that date, it will be returned without review. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

#### REVIEW CONSIDERATIONS

##### Review Procedure

Upon receipt, applications will be reviewed for completeness by the DRG and responsiveness by the NCI. Incomplete applications will be returned to the applicant without further consideration. Applications that are judged to be non-responsive will be returned by the NCI. Applications judged to be non-responsive to this RFA may be submitted as an investigator initiated regular research grant (R01) or program project grant (P01) at the next receipt date. The application would require modification in accordance with R01 or P01 guidelines. The revised application would not be considered an application for a cooperative agreement nor would it be considered a response to an RFA. Questions concerning the responsiveness of proposed research to the RFA are to be directed to the program staff listed under INQUIRIES.

Applications may be triaged by an NCI peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will undergo further scientific merit review. Those applications that are complete and responsive will be evaluated in accordance with the criteria for scientific/technical review by an appropriate peer review group convened by the Division of Extramural Activities, NCI. The second level of review will be provided by the National Cancer Advisory Board.

#### INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA and inquiries about whether or not specific proposed research would be responsive are strongly encouraged and should be directed to the program staff listed below. The program staff welcome the opportunity to clarify any issues or questions from potential applicants.

Direct inquiries regarding programmatic issues and requests for the RFA to:

Dr. David Parkinson, Chief Investigational Drug Branch  
Cancer Therapy Evaluation Program  
National Cancer Institute  
Executive Plaza North, Room 734  
Bethesda, MD 20892  
Telephone: (301) 496-5223  
FAX: (301) 480-4663

Direct inquiries regarding fiscal matters to:

Barbara A. Fisher  
Grants Management Specialist  
National Cancer Institute  
Executive Plaza South, Room 242  
Bethesda, MD 20892  
Telephone: (301) 496-7800, ext. 29  
FAX: (301) 496-8601

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No 93.395, Cancer Treatment Research. Awards are made under the authorization of the Public Health Service Act, Title IV Sections 301, 410, and 411, Part A (Public Law 78-410, 42 USC 241 as amended, Public Law 99-158, 42 USC 285a) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

RFA AVAILABLE: AI-93-07

P.T. 34; K.W. 0710070, 0715015

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: January 15, 1993

Application Receipt Date: March 25, 1993

THE REQUEST FOR APPLICATION (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACTS NAMED IN INQUIRIES, BELOW.

#### PURPOSE

The Division of Allergy, Immunology and Transplantation (DAIT) of the National Institute of Allergy and Infectious Diseases (NIAID) invites applications for studies dealing with the mechanisms of peripheral immunological tolerance and anergy. Improved knowledge of peripheral tolerance and anergy is likely to open new avenues to treatment or prevention of a variety of autoimmune and allergic disorders, to moderating organ and bone marrow graft rejection, and to approaches for vaccination against infectious organisms.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Mechanisms of Peripheral Immunological Tolerance and Anergy, is related to the priority areas of diabetes and chronic disabling diseases, and to immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-782-3238).

#### ELIGIBILITY REQUIREMENTS

Only domestic organizations are eligible to apply. Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. The NIAID encourages the participation of minorities and women, either as the Program Director or as project leaders of the component research projects of the application.

#### MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Program Project grant (P01). The P01 is an assistance mechanism for the support of broadly based, multidisciplinary, long-term research programs with a specific major goal or central theme and generally involving the organized efforts of groups of investigators. Applicants will be solely responsible for the planning, direction, and execution of the proposed project. The total project period may not exceed five years. The budget of the P01 application should not exceed \$500,000 total direct costs and no more than four percent annual inflationary increases for future years. Budget requests exceeding this amount will require written approval by senior NIAID officials through the program officer before the application is accepted for review.

#### FUNDS AVAILABLE

The estimated total funds (direct and indirect costs) available (direct and indirect costs) for the first year of support for this RFA is \$1,500,000. In Fiscal Year 1993, the NIAID plans to award at least two program project grants submitted in response to this RFA and, depending on availability of funds and scientific merit, possibly more than two. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIAID, awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and availability of funds.

#### RESEARCH OBJECTIVES

The goal of this program is to gain a comprehensive understanding of the nature of peripheral tolerance and anergy: what they are, how they are induced, and the biochemical and molecular genetic events involved in inducing and maintaining them. The following are some examples of the questions about T lymphocytes that need to be addressed:

- o What are the elements (e.g., types of interacting cells, surface molecules, cytokines) and mechanisms involved in T cell tolerance and anergy that operate extrathymically?
- o Do the mechanisms that lead to tolerance and anergy differ depending on the tolerizing/anergizing stimulus? For example, would the mechanisms differ if a conventional antigen or a super-antigen were involved, or if the stimulus were a free peptide compared to a Class II-peptide complex?
- o What roles are played by the Ti-CD3 complex or by CD4 and CD8 accessory molecules in the induction of T cell tolerance?



o Are CD4+ and CD8+ T cells distinguishable in their susceptibility to the induction of tolerance and anergy?

o What are the different roles played by TH1 and TH2 cells and the spectra of cytokines that they secrete in the induction and maintenance of tolerance and anergy?

The following are some examples of questions about B lymphocytes that need to be addressed:

o What is the importance of the density, distribution, affinity and isotype of membrane-bound antibody molecules?

o Is B-cell anergy associated with the absence of stimuli/signals that would otherwise lead to B-cell activation and, if so, what is the nature of such stimuli?

o What is the importance of the differentiative status of B cells in terms of the induction of tolerance and anergy?

#### STUDY POPULATIONS

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit by, January 15, 1993, a letter of intent that includes a descriptive title of the overall proposed research, the name, address and telephone number of the Program Director; the names of key investigators (project leaders), their institution(s), and the number and title of this RFA. (The NIAID encourages the consideration of one junior scientist to lead one of the projects but who will work closely with one or more senior scientists in the program project: see full RFA). Although the letter of intent is not required, is not binding, does not commit the sender to submit an application, and does not enter into the review of subsequent applications, the information that it contains allows NIAID staff to estimate the potential review workload and to avoid conflict of interest in the review. The letter of intent is to be sent to Dr. Mark Rohrbach at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

Applications are to be submitted on the research project grant application form PHS 398 (rev. 09/91). Item 2a on the face page of the application must be marked "yes" and the RFA number and the words "MECHANISMS OF PERIPHERAL IMMUNOLOGICAL TOLERANCE AND ANERGY" must be typed in.

These forms may be obtained from most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441.

Applications must be received by March 25, 1993.

#### REVIEW CONSIDERATIONS

General review considerations are outlined in the NIAID Information Brochure on Program Project and Center Grants which contains special instructions for preparing multi-project applications. It includes REVIEW PROCEDURES and REVIEW CRITERIA for multi-component interdisciplinary projects and other important information. This Information Brochure and the RFA will be sent to applicants upon request.

Upon receipt, applications will be reviewed for completeness by the Division of Research Grants (DRG) and for responsiveness by NIAID staff; those judged to be incomplete or non-responsive will be returned to the applicant without review.

Those applications that are complete and responsive may be subjected to a triage by an NIAID peer review group before or during the scientific review meeting to determine their scientific merit relative to other applications received in response to this RFA. The NIAID will withdraw from competition those applications judged to be non-competitive for award and will notify the applicant and institutional business officials.

Those applications judged by the reviewers to be competitive for award will be further reviewed for scientific and technical merit by a review committee convened by the Division of Extramural Activities, NIAID. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council.

#### AWARD CRITERIA

Funding decisions will be made on the basis of scientific and technical merit as determined by peer review, program needs and balance, and the availability of funds.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcomed.

Direct requests for the RFA and Information Brochure, as well as inquiries regarding programmatic issues to:



Joseph F. Albright, Ph.D. or M. Michele Hogan, Ph.D.  
Division of Allergy, Immunology and Transplantation  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4A22  
Bethesda, MD 20892  
Telephone: (301) 496-7551  
FAX: (301) 402-0175

Send the letter of intent and direct inquiries regarding review issues to:

Mark L. Rohrbaugh, Ph.D.  
Microbiology & Immunology Review Section  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4C22  
Bethesda, MD 20892  
Telephone: (301) 496-8424  
FAX: (301) 402-2638

Direct inquiries regarding fiscal matters to:

Mr. Jeffrey Carow  
Grants Management Branch  
Division of Extramural Activities  
National Institute of Allergy and Infectious Diseases  
Solar Building, Room 4B29  
Bethesda, MD 20892  
Telephone: (301) 496-7075

The mailing address for sending applications to NIAID staff in the Solar Building is the central mailing address for the NIH. Applicants who use express mail or a courier service are advised to follow the carrier's requirements for showing a street address. The address for the Solar Building is:

6003 Executive Boulevard  
Rockville, MD 20852

#### Schedule

Letter of Intent Date: January 15, 1993  
Application Receipt Date: March 25, 1993  
Scientific Review Date: June 1993  
Advisory Council Date: September 1993  
Earliest Award Date: September 1993

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.855 - Immunology, Allergy and Transplantation Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### KIDNEY RESEARCH CENTERS

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFA AVAILABLE: DK-93-09

P.T. 04; K.W. 0785095, 1002004, 1002008, 0710070, 1002019, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: March 8, 1993  
Application Receipt Date: April 9, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

#### PURPOSE

This RFA invites investigators to submit research applications for the George M. O'Brien Research Centers Program. The emphases for this program are threefold: (1) to attract new scientific expertise into the study of the basic mechanisms of kidney diseases and disorders; (2) to encourage multidisciplinary research focused on the causes these diseases; and (3) to extend the development of innovative clinical and epidemiologic studies of the causes, therapy and possible prevention of kidney diseases and disorders. In approaching the study of these disease processes, it is anticipated that extensive collaboration will be required between individuals in the clinical and basic sciences, including, for example, investigators with training and expertise in cell biology, molecular biology, immunology, genetics, epidemiology, biochemistry, physiology, and pathology. It is the express intent of the announcement to attract new investigators not currently active in this field and to explore new basic areas that may have clinical research applications. Individual institutions with both basic and clinical research capabilities are eligible to apply. Interinstitutional collaborative research

arrangements are also appropriate and encouraged. Coordination for such arrangements must be evident and clearly meaningful and appropriate for the research proposed.

#### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Kidney Research Centers, is related to the area of diabetes and other chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and nonprofit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible to apply. Minority individuals and women are encouraged to submit as principal investigators.

#### MECHANISM OF SUPPORT

Support of this program will be through the National Institutes of Health (NIH) specialized center (P50) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this announcement, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement.

#### FUNDS AVAILABLE

The NIDDK expects to award up to two center grants (P50) in FY 1993 for research into kidney disorders. The anticipated awards are for five years and are contingent upon the availability of appropriated funds. The total amount of available funds to support this program is anticipated to be no more than \$1.5 million per year. No applicant may request more than \$750,000 (including both direct and indirect costs) in total costs in the initial budget period. A standard escalation factor may be used for subsequent budget periods. The award date for these grants will be September 30, 1993.

#### SPECIAL REQUIREMENTS

Successful applicants are expected to attend a yearly meeting of Center Directors convened by the NIDDK. Funds to support travel to this meeting may be requested in the budget proposed for the center.

#### STUDY POPULATIONS

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them. The study design must seek to identify any pertinent gender or minority population differences.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations, a specific justification for his exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by March 8, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

A letter of intent is not required, is not binding, and does not enter into the review of subsequent applications.

The letter of intent is to be sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083  
FAX: (301) 402-1277

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. The form is available from most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone 301/496-7441.

The RFA label available in the application form must be affixed to the bottom of the face page. Detailed instructions on submission procedures are described in the RFA.

#### REVIEW CONSIDERATIONS

Upon receipt, applications will be initially reviewed for completeness and responsiveness. Incomplete applications or non-responsive applications will be returned to the applicant without further consideration.

Those applications that are complete and responsive will be evaluated in accordance with the usual NIH peer review procedures. Following this review, the applications will be given a secondary review by the NIDDK Advisory Council unless not recommended for further consideration by the initial review group.

#### INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.

Inquiries regarding programmatic issues and requests for copies of the RFA may be directed to:

Ralph L. Bain, Ph.D.  
Director, Centers Program  
Division of Kidney, Urologic, and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A-05  
Bethesda, MD 20892  
Telephone: (301) 496-7574

Inquiries regarding fiscal matters may be directed to:

Ms. Helen Ling  
Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.849. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

#### UROLOGY RESEARCH CENTERS

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFA AVAILABLE: DK-93-21

P.T. 04; K.W. 0785220, 1002004, 1002008, 0710070, 1002019, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases  
The National Cancer Institute

Letter of Intent Receipt Date: March 8, 1993  
Application Receipt Date: April 9, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRES, BELOW.

#### PURPOSE

This RFA invites investigators to submit research applications for the George M. O'Brien Research Centers Program. The emphases for this program are threefold: (1) to attract new scientific expertise into the study of the basic mechanisms of urological diseases and disorders; (2) to encourage multidisciplinary research focused on the causes of these diseases and disorders; and (3) to extend the development of innovative clinical and epidemiologic studies of the causes, therapy and possible prevention of urological diseases and disorders. In approaching the study of these disease processes, it is anticipated that extensive collaboration will be required between individuals in the clinical and basic sciences, including for example investigators with training and expertise in cell biology, molecular biology, immunology, genetics, epidemiology, biochemistry, physiology, and pathology. It is the express intent of the announcement to attract new investigators not currently active in this field and to explore new basic areas that may have clinical research applications. Individual institutions with both basic and clinical research capabilities are invited to apply. Interinstitutional collaborative research arrangements are also appropriate and encouraged. Coordination for such arrangements must be evident and clearly meaningful and appropriate for the research proposed.

The National Cancer Institute (NCI) plans to provide support for this program in the area of prostate cancer.

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Urology Research Centers, is related to the area of diabetes and other chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible to apply. Minority individuals and women are encouraged to submit as principal investigators.

#### MECHANISM OF SUPPORT

Support of this program will be through the National Institutes of Health (NIH) specialized center (P50) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this announcement, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement.

#### FUNDS AVAILABLE

The NCI and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) expect to jointly award up to two center grants (P50) in fiscal year 1993 for research into urologic disorders. The anticipated awards are for five years and are contingent upon the availability of appropriated funds. The total amount of available funds to support this program is anticipated to be no more than \$1.5 million per year. No applicant may request more than \$750,000 (including both direct and indirect costs) in total costs in the initial budget period. A standard escalation factor may be used for subsequent budget periods. The award date for these grants will be September 30, 1993.

#### SPECIAL REQUIREMENTS

Successful applicants are expected to attend a yearly meeting of Center Directors convened by the NIDDK. Funds to support travel to this meeting may be requested in the budget proposed for the center.

#### STUDY POPULATIONS

It is NIH policy that women and minorities must be included in clinical study populations unless there is a good reason to exclude them. The study design must seek to identify any pertinent gender or minority population differences.

#### SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations, a specific justification for his exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by March 8, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

A letter of intent is not required, is not binding, and does not enter into the review of subsequent applications.

The letter of intent is to be sent to:

Chief, Review Branch  
Division of Extramural Activities  
National Institutes of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 605  
Bethesda, MD 20892  
Telephone: (301) 496-7083  
FAX: (301) 402-1277

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. The form is available from most institutional offices of sponsored research and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone (301) 496-7441.

The RFA label available in the application form must be affixed to the bottom of the face page. Detailed instructions on submission procedures are described in the RFA.



## REVIEW CONSIDERATIONS

Upon receipt, applications will be initially reviewed for completeness and responsiveness. Incomplete applications or non-responsive applications will be returned to the applicant without further consideration.

Those applications that are complete and responsive will be evaluated in accordance with the usual NIH peer review procedures. Following this review, the applications will be given a secondary review by the National Diabetes and Digestive and Kidney Diseases Advisory Council and the National Cancer Advisory Board unless not recommended for further consideration by the initial review group.

## INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.

Inquiries regarding non-cancer programmatic issues and requests for copies of the RFA may be directed to:

Ralph L. Bain, Ph.D.  
Director, Centers Program  
Division of Kidney, Urologic, and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 3A-05  
Bethesda, MD 20892  
Telephone: (301) 496-7574

Inquiries regarding cancer related programmatic issues and requests for the RFA may be directed to:

Andrew Chiarodo, Ph.D.  
Chief, Organ Systems Coordinating Branch  
Centers, Training, and Resources Program  
Division of Cancer Biology, Diagnosis and Centers  
National Cancer Institute  
Executive Plaza North, Suite 316  
Bethesda, MD 20892  
Telephone: (301) 496-8528

Inquiries regarding fiscal matters may be directed to:

Ms. Helen Ling  
Grants Management Specialist  
Division of Extramural Activities  
National Institute of Diabetes and Digestive and Kidney Diseases  
Westwood Building, Room 649  
Bethesda, MD 20892  
Telephone: (301) 496-7467

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.849. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ASTHMA CLINICAL RESEARCH NETWORK

NIH GUIDE, Volume 21, Number 45, December 18, 1992

RFA AVAILABLE: HL-93-11-L

P.T. 34; K.W. 0715013, 0745070, 0755018

National Heart, Lung, and Blood Institute

Letter of Intent Receipt Date: March 1, 1993

Application Receipt Date: May 6, 1993

THE REQUEST FOR APPLICATIONS (RFA) ANNOUNCED IN THIS NOTICE CONTAINS ESSENTIAL INFORMATION FOR THE PREPARATION OF AN APPLICATION. POTENTIAL APPLICANTS MAY OBTAIN THE RFA FROM THE CONTACT NAMED IN INQUIRIES BELOW.

## PURPOSE

The Division of Lung Diseases invites applications for four Clinical Groups and one Data Coordinating Center to participate, with the assistance of the National Heart, Lung, and Blood Institute (NHLBI), in the establishment of a network of interactive asthma clinical research groups designed to facilitate evaluation of novel treatment methods and management strategies for asthma; and to rapidly disseminate the findings from these clinical studies to the health care community. This RFA is to: (1) provide a mechanism to establish and maintain the infrastructure required to perform multiple therapeutic trials of novel treatments and management strategies for asthma using common protocols with the requisite numbers of patients. Support would be provided to maintain the infrastructure with additional funds provided on a cost per patient basis for conducting clinical protocols. (2) Establish a Data Coordinating Center for the network. The solicitation is for five years.

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Asthma Clinical Research Network, is related to the priority areas of chronic disabling conditions and clinical prevention services. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

#### ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign organizations are not eligible to apply and domestic applications may not include international components. Applications from minority individuals and women are encouraged.

#### MECHANISM OF SUPPORT

The administrative and funding mechanism to be used to undertake this program will be a cooperative agreement (U01), an assistance mechanism. Under the cooperative agreement, the NIH assists, supports, and/or stimulates and is substantially involved with recipients in conducting a study by facilitating performance of the effort in a "partner" role. The anticipated award date is September 30, 1993.

#### FUNDS AVAILABLE

An estimated four awards for Clinical Groups and one award for a Data Coordinating Center will be made under this RFA. A maximum of about \$17.4 million (including direct and indirect costs) over a five-year period will be awarded for the Clinical Groups and the Data Coordinating Center. Approximately \$2.50 million will be available for the first year, \$3.5 million for the second year, \$3.6 million for the third year, \$3.8 million the fourth year and \$3.9 million for the last year. It is anticipated that the award for each Clinical Group will be about \$475,000 total costs for the first year and the award for the Data Coordinating Center will be about \$600,000 total costs for the first year. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will also vary in all years. Future year costs will be distributed based on the recommended protocols.

At this time the NHLBI anticipates that there will be a renewed competition after five years. However, the final decision will depend upon experience with the network during the first five years as well as financial considerations.

#### RESEARCH OBJECTIVES

Asthma is an increasingly serious cause of morbidity and mortality in the United States. There are approximately 12 million asthmatics in this country. The disease affects both sexes and impacts all racial/ethnic groups. Despite major advances in understanding the etiology and pathophysiology of asthma and the development of new therapeutic modalities, the prevalence, severity, and mortality from asthma have increased over the past decade in all age groups. In addition to the rise in morbidity and mortality, hospitalizations for asthma have doubled in adults and increased fivefold for children over the past 20 years. Mortality rates appear to be particularly high in urban and rural minority populations. Asthma continues to place a heavy burden on patients and their families, the health care system, and society as a whole. Therefore, new approaches are needed to help alleviate this growing problem.

One important need is to establish a mechanism to allow rapid evaluation of new and existing therapeutic approaches for asthma, and for dissemination of laboratory and clinical findings to the health care community. This program seeks to accomplish this through a network of interactive asthma clinical groups that conduct clinical research in a coordinated and multidisciplinary setting.

The objective of this initiative is to establish a network of interactive asthma clinical research groups to rapidly assess novel treatment methods, and to ensure that these findings on optimal management of asthmatic patients are rapidly disseminated to practitioners and health care professionals. This program is intended to provide a mechanism to establish and maintain the required infrastructure to perform multiple therapeutic trials in asthmatic patients. It is envisioned that the Clinical Groups would have significant experience and a strong history of basic and clinical research on the pathogenesis and treatment of asthma, since the program infrastructure should be built around existing research projects. Therefore, it will be advantageous for groups to have had substantial previous basic and/or clinical research experience in asthma and asthma related fields.

The study population is envisioned to be asthmatic patients encompassing a broad range of age groups and consisting of appropriate gender and minority representation with clearly defined and documented asthma. At a minimum, one third of the patient population at each clinic should be minority individuals and one half women. It is expected that each Clinical Group will have the ability to access at least 400 patients for various protocols over the five year period, but it is not envisioned that all 400 patients would necessarily be enrolled in research protocols at any one time, and it is possible that an individual patient may be involved in more than one study. Of the total patients accessible, investigators should include substantial numbers from a broad age range, as well as a description of the age distribution, and characteristics of the population that they might recruit into potential clinical trials.

The overall population to be studied should provide data that are broadly applicable to diverse minority groups as well as whites; thus, the composition of the study population in this RFA program must reflect this diversity.

The timetable for the network may be roughly subdivided into three phases over a five year period. Phase I consists of the first twelve months and may be devoted to planning, development of the network infrastructure,

and protocol development. In Phase II, protocol development continues, patient recruitment and protocol implementation are estimated to proceed over a 48-month period. Phase III will consist of data analysis, report preparation, closeout of the initial studies, further protocol development, continued recruitment for the next studies, which may proceed over approximately a 36-month period.

#### STUDY POPULATIONS

##### SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, the NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by March 1, 1993, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NHLBI staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. C. James Scheirer at the address listed under INQUIRIES.

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone (301) 496-7441; and from the NIH Project Scientist named below.

Applications must be received by May 6, 1993. If an application is received after this date it will be returned to the applicant without review.

#### REVIEW CONSIDERATIONS

Applicants are encouraged to submit and describe their own ideas on how best to meet the goals of the study, but they are expected to address issues identified under SPECIAL REQUIREMENTS of the RFA. Note that this document is not the RFA. Applications will be judged primarily on the scientific quality of the application. Although the technical merit of the protocol is important, it will not be the sole criterion for selection of a Clinical Group. Other considerations such as the importance and timeliness of the proposed clinical trials, access to patients, multidisciplinary nature of the study, the discussion of considerations relevant to this RFA, expertise of the investigators, their capability to perform the work proposed, and a demonstrated willingness to work as part of the network and with the NHLBI Project Scientist will be part of the evaluation criteria.

The review group will assess (as further detailed in the RFA):

##### Clinical Groups

- o Scientific merit of the proposed clinical trials.
- o Qualifications, experience, and commitment of key personnel, including their previous experience conducting clinical research in asthma.
- o Plans to recruit an adequate number of patients, including appropriate representation of minorities and women.
- o Facilities, equipment and organizational structure to effectively implement protocols through the network.
- o Rationale and cost-effectiveness of the research approach proposed.

##### Data Coordinating Center

- o Scientific merit of the proposed clinical trials.
- o Organizational, administrative, and supervisory ability and statistical expertise to serve as a Data Coordinating Center for multiple multicenter randomized controlled clinical trials in asthma.
- o Qualifications, experience, and commitment of key personnel.
- o Facilities and equipment to function as a Data Coordinating Center for a multicenter network.
- o Appropriateness of the budget for the work proposed.

## AWARD CRITERIA

Applications recommended by the National Heart, Lung, and Blood Advisory Council will be considered for award based upon (a) scientific and technical merit, importance of the proposed clinical trials, timeliness, multidisciplinary nature of the study, and the requirements explicitly stated in this RFA; (b) program balance, including in this instance, sufficient compatibility of features to make a successful collaborative program a reasonable likelihood; and (c) availability of funds.

Letter of Intent: March 1, 1993  
Application Receipt Date: May 6, 1993  
Review by NHLBAC: September 1993  
Anticipated Award Date: September 30, 1993

## INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Inquiries regarding this announcement and requests for the RFA may be directed to:

James P. Kiley, Ph.D.  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 6A15  
Bethesda, MD 20892  
Telephone: (301) 496-7332  
FAX: (301) 496-9886

Inquiries regarding review and application procedures may be directed to:

C. James Scheirer, Ph.D.  
Review Branch, Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 648  
Bethesda, MD 20892  
Telephone: (301) 496-7363  
FAX: (301) 402-1660

Inquiries regarding fiscal and administrative matters may be directed to:

Mr. Raymond L. Zimmerman  
Grants Operations Branch  
Division of Extramural Affairs  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 4A11C  
Bethesda, MD 20892  
Telephone: (301) 496-4970  
FAX: (301) 402-1200

## AUTHORITY AND REGULATIONS

This project is described in the Catalog of Federal Domestic Assistance No. 93.837. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR 74. This project is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## ONGOING PROGRAM ANNOUNCEMENTS

### NATIONAL CANCER INSTITUTE/MINORITY ACCESS TO RESEARCH CAREERS SUMMER TRAINING SUPPLEMENT

NIH GUIDE, Volume 21, Number 45, December 18, 1992

PAR NUMBER: PAR-93-33

P.T. 34, FF; K.W. 0715035, 0720005

National Cancer Institute

Application Receipt Date: February 1, 1993

## PURPOSE

The Comprehensive Minority Biomedical Program (CMBP) of the Division of the Extramural Activities (DEA), National Cancer Institute (NCI), invites interested grantee institutions that have Minority Access to Research Careers (MARC) grants to apply for CMBP support of MARC scholars interested in obtaining laboratory research experience at the NCI. This program announcement will be reissued on an annual basis.

The NCI, through a co-funding arrangement with the MARC program of the National Institute of General Medical Sciences (NIGMS), provides support for research training to minority individuals and institutions and conference



grant support to further address and enhance the mission of the National Cancer Program. The NCI/MARC Summer Training Program is an extension of the co-funding process.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Health People 2000," a PHS-led national activity for setting priority areas. This program announcement, NCI/MARC Summer Training Supplement, is related to the priority area of cancer research. Potential applicants may obtain a copy of "Health People 2000" (Full Report: Stock No. 017-001-00474-0) or (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

## ELIGIBILITY CRITERIA

All domestic institutions with active MARC research training grants are eligible to apply.

## MECHANISM OF SUPPORT

A MARC honors training grant (T34) to the academic institution requesting support for a student will be administratively supplemented. Unless otherwise noted, all PHS and NIH grants policies apply to applications received in response to this announcement.

The supplement will provide the following: (1) A subsistence of \$300 per week (\$3,000 for a maximum ten-week period), and (2) round-trip transportation (from MARC student's academic institution to the National Institutes of Health, Bethesda, Maryland, and return to student's academic institution). Indirect costs may be awarded to the institution for up to a maximum of eight percent of the direct costs.

## RESEARCH OBJECTIVES

The purpose of this award is to increase research training opportunities in the NCI for underrepresented minority scholars and to increase the number of minority scholars entering cancer-related research careers through the influence of short-term laboratory training at the NCI.

## APPLICATION PROCEDURES

The Principal Investigator must submit a letter, countersigned by an authorizing official of the grantee institution, requesting support of a student for short-term laboratory training at the NCI. This letter will constitute an application and must include the following:

- o A statement from the student that describes his/her research interests and career objectives and a brief resume;
- o Two letters of recommendation;
- o A current official college/university transcript;
- o The student's selection of three NCI laboratory choices prioritized by level of interest;
- o The title of the announcement;
- o A copy of the face page of the active MARC grant including the grant number and period of award; and
- o A description of the personnel to which the student will report his/her NCI laboratory experience.

A list of NCI laboratory choices will be available to all applicants through the CMBP office.

Application packages must be received by the CMBP no later than February 1, 1993.

The 10-week training period may be between May 1993 and August 1993, inclusive. Under this announcement funding is available for this period only.

More than one supplemental application may be submitted by each grantee institution.

Supplemental applications to active MARC undergraduate training grants must be submitted directly to the CMBP, with a copy to the MARC program, at the address listed below.

## REVIEW CONSIDERATIONS

Applications in response to this announcement will be considered by NCI Staff; final selection for laboratory experience will be made by the relevant laboratory directors. Selection will be made on the following criteria:

- o The strength of the interest in pursuing a laboratory experience in the biomedical sciences based on the statement from the student;
- o The strength of the letters of recommendation;
- o Cumulative grade point average (2.75 or more based on 4.0 maximum).

Applications found to be responsive to the announcement will be considered; those found to be unresponsive will not be considered. A letter from the CMBP Director will be sent to the grantee institution stating the reason for the outcome of the evaluation.

## INQUIRIES

Direct inquiries regarding programmatic issues to:

Program Director  
Comprehensive Minority Biomedical Program  
Division of Extramural Activities  
National Cancer Institute  
Building 31, Room 10A04  
Bethesda, MD 20892  
Telephone: (301) 496-7344



Program Director  
Minority Access to Research Careers  
National Institute of General Medical Sciences  
Westwood Building, Room 9A18  
Bethesda, MD 20892  
Telephone: (301) 496-7941

Direct inquiries regarding fiscal matters to:

Ms. Carolyn Mason  
Grants Management Specialist  
Grants Administration Branch  
National Cancer Institute  
Executive Plaza South, Room 243  
Bethesda, MD 20892  
Telephone: (301) 496-7800, Extension 59

## AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.398 Cancer Research Manpower. National Institutes of Health, Public Health Service, Department of Health and Human Services Authorization: Public Health Service Act, Service 413, as amended by Public Law 99-158, 42 U.S.C. 288. Federal Agency: National Institutes of Health, Public Health Service, Department of Health and Human Service Authorization: Public Health Service Act, Section 301, Public Law 78- 410, 42 U.S.C. 241, and Section 412, as amended by Public Law 99-158, 42 U.S.C. 285a-1. Executive Order 12372 applicable.

## ERRATUM

### "FAILURE TO THRIVE" SYNDROME AMONG OLDER PERSONS

NIH GUIDE, Volume 21, Number 45, December 18, 1992

PA NUMBER: PA-93-22

P.T. 34; K.W. 0710010, 0710095, 0715072, 0710070, 0765035

National Institute on Aging  
National Institute of Mental Health

This erratum is issued for Program Announcement PA-93-22, published in the NIH Guide for Grants and Contracts, Vol. 21, No. 42, November 20, 1992. There are two staff changes under the section INQUIRIES.

## INQUIRIES

James K. Cooper, M.D., Geriatrics Program, Suite 3E327  
Telephone: (301) 496-6761

Pamela Starke-Reed, Ph.D., Biology of Aging Program, Suite 2C231  
Telephone: (301) 496-6402

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:**

5333 Westbard Avenue  
Bethesda, MD 20816









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